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Editorial

The position of the physician in society is constantly changing. In ancient Egypt he had the status of a priest, in the era of the Roman Empire he was a lowly slave, and during the Middle Ages he was a satellite of a titled personage. Nowadays the physician is a business man engaged in free competition with other members of his profession. It is only to be expected that this will give way to another position as society changes or its demands for medical care change. Thus it is a great mistake to regard medicine as a science quite separate from the social and political organization of a state.

American medicine has undergone a great development in the last fifty years. From a relatively backward condition it has developed until now it equals or surpasses European medicine in many fields. This advancement has been in the scientific side of medicine, not in its social side, and although now abler than ever before to prevent disease and aid the sick, medicine is not taking full advantage of its knowledge. It has been held that this discrepancy between the technical advances and the lack of social advances in medicine will be corrected in the natural course of events, but such a process is always very slow and painful.

It does not require a very astute mind to realize that any politico-social organization which intermittently has great wars and periodically throws enormous numbers of people out of work, is basically unsound. Neither does it require much thought to realize a medical organization which gives expensive treatment to the rich and poor treatment to the poor, is basically unsound.

Many influences are acting upon the medical profession and these will increase. When the rich realize they are being over-charged and the poor realize they are not getting the adequate care that they should get, these influences are certain to increase. The medical organization will change with new social demands and it seems to be a question of whether international medicine is going to co-operate with or oppose these demands. Some quarters believe that the medical societies have become reactionary organizations to protect the interests of the doctor, and his pocket-book, instead of a means of bringing the best medical care to the largest number of people. The recent indictment of the American Medical Association increased this belief in the minds of many.

It appears that the present system of medical service is inadequate. Phy-

sicians will not go to the sparsely settled districts because they cannot make a living. The result is an acute need of doctors in these areas. The conditions in the more heavily populated districts are no better. Many doctors are barely eking out an existence and yet there are thousands of patients who need a doctor and are barred financially. It is true that the medical profession gives more real aid to the poor than the State, but this is not a condition for charity. It is too big for charity.

The supporters of socialized medicine have many suggestions that are worthy of thoughtful survey. They point out that State control is not a new departure in medicine. Over half the hospital beds are owned and operated by the State and the economic depression has increased this trend. Medicine expects the state to take over increasing duties in the care of the indigent sick, the mentally ill, the tuberculous, the blind and the deaf.

A highly trained and intelligent medical profession, with its tradition of independent thought and action, actively oppose any political control. Medicine fears that it would become a political foot-ball and be open to patronage, graft, and inefficiency, as reflected in many government controlled organizations. The advocates of socialized medicine maintain that the average man is too keenly interested in medicine to allow such conditions to appear in a service which affects him so personally. He may be quite indifferent to the efficiency and graft of highway construction but he cannot afford to be indifferent to his medical service.

The free choice of doctor by patient is held to be all important by the supporters of the status quo who maintain there is more confidence in, and better co-operation with, the doctor freely chosen. Yet on the other hand, the majority of people do not have a truly free choice of doctor now. The poor attending free clinics accept the doctor they chance to get. Miners, bush workers, saw-mill hands, have to take the company doctor. People in outlying districts usually only have one doctor to call. The city dweller who can afford it usually calls the doctor who is handiest.

The personal doctor-patient relationship is another point of difference. All agree that this personal relationship must be maintained, as the intervention of a third party would not permit the free confidences that are necessary. The proponents of socialized medicine say that a third figure would not be introduced into the picture. They hold that the money question spoils this relationship now, as the doctor must sell himself to the patient and impress the patient that he is a "good doctor," in order to keep the patient.

The opponents maintain that salaried doctors would lose their incentive. The proponents point out that some of the greatest medical workers have been salaried men and that the desire of personal distinction in the eyes of the profession is just as great an incentive as money. Certainly, they hold, money cannot be a major incentive in medicine since the average income of the physician is only $3,500.00 per annum. The salary system of reimbursement would tend to decrease unnecessary surgery or expensive treatment. Also under this system doctors would have regular holidays and be urged to attend periodic post graduate courses, both of which would increase the efficiency of the profession.

All these problems are of real interest to the medical profession. The individual physician is not in favour of any radical change. He does not want to become a government employee and lose much of his independence. But whether or not socialized medicine will evolve depends largely upon the influences acting on the medical profession. Medical organization is changing with the social conditions. The next fifty years will likely see great advances in the social organization of medicine.

INFECTIONS IN HANDS

By J. HAROLD COUCH, M.A., F.R.C.S.
Department of Surgery, University of Toronto

Infection in hands can be avoided. Therefore, the blame for the long and costly illness and the permanent disability which follows must be laid at someone's door. Sometimes it is the patient who is to blame and sometimes it is the doctor; but always there is someone.

Infection never occurs spontaneously. It arises because bacteria gain entrance to tissue through some portal. Over 100 years ago Spallanzani following in the footsteps of Leeuwenhoek, proved that pus which appeared in wounds was not generated spontaneously but was the result of the introduction of living organisms into the wound. Lister argued that if this were true, he would attack those organisms and prevent their entry so he built the carbolic spray. To-day, we sometimes forget the teaching of these great men, although their statements are just as true and just as useful as when first made.

If bacteria could be prevented from establishing themselves, infected hands would not occur. Furthermore, the portal of entry is usually so obvious that it can easily be safeguarded. Bacteria enter through breaks in the epithelium. Blood borne infection in hands is practically unknown. All infections were, at their earliest stage, simply wounds. Therefore, an infected hand means a neglected hand. Someone had a chance to cleanse the wound vigorously and so ensure primary healing.

From the patient's view point, it is easy to understand carelessness. Most small wounds do not become infected, even though infections do begin in wounds. Ninety-nine times out of a hundred no serious consequences follow small injuries.

Workers must be taught, and are being taught, that the one time when infection does lodge is so costly and so serious, both to the individual and to organized industry, that care must be taken to avoid it.

What can the workman do? Most large plants to-day come under the Workmen's Compensation Board, and have set up first aid posts with a first aid man in charge who has had some training. The men are instructed to report promptly all injuries, large or small. This gives the first aid man a chance to cleanse the wound and apply dressing.

If there is no such station available, the injured man might well follow the simple routine employed by some surgeons in the event of accidental wounding of the finger by a needle while operating on an infected case. At the earliest possible moment, the surgeon scrubs the wound vigorously for several minutes with soap and water and a small scrub brush such as is used before operation. He then applies an antiseptic, perhaps iodine. It sounds simple and yet it must be efficacious because a good hand is important to a surgeon — just as important as it is to a machine worker. Where workers are grouped together, instruction may be given in their responsibility in caring for small wounds early.

But the doctor also has a part in the picture for sometimes the patient does present himself promptly after injury, and then the responsibility for cleansing the wound thoroughly and obtaining primary union rests solely with the doctor.

GENERAL PRINCIPLES

By way of general remarks, applicable to all cases, one or two first principles may be laid down, before going on to details of specific conditions.

1. Thorough Operation:

If operation is undertaken at all, it must be performed thoroughly. More harm is done by inadequate stabs in an infected hand than would be done by leaving it alone altogether. We have seen a patient with a "frozen hand" like a small ham, who had had 20 incisions, none of them over ½ in. long. The hand was a total loss from the point of view of function.

Incision should be made directly over the place where pus is most certain to be found, and then should follow wherever the pus leads. Counter openings are made at appropriate places to ensure free and adequate drainage.

A little knowledge is a dangerous thing, in hands as elsewhere. A knowledge of anatomy may result in more harm than good. Surgeons have been known to demonstrate and save the arterial arches at the expense of good drainage. The whole hand became fibrosed and useless. Once infection has lodged it is a "sine qua non" that the infection must be overcome, and that as promptly as possible.

Prolonged infection produces fibrosis, widespread throughout the whole hand. The correct knowledge of anatomy suggests that the surgeon should sacrifice anything which is necessary to secure free drainage at the *first* operation, making exception only of nerves and tendons.

Motor nerves must not be cut. Reference is particularly to the motor branch of median running to thenar eminence as well as ulnar branches which are equally important but less exposed. The statement that tendons must not be cut, nor sheaths opened, is so obvious as barely to require mention. Both of these "thou shalt nots" are easily respected by the usual incisions running in direction of important structures.

2. Tourniquet:

Operations on hands should always be performed under tourniquet. A clean bloodless field permits accurate anatomical dissection and gentle accomplishment of the task. Operation will be more thorough and less traumatic.

In cases limited to the distal half of the finger, an elastic band placed once around the base of finger and held with forcep is excellent. A regular pneumatic tourniquet above elbow will be necessary for all operations on body of hand or wrist.

3. Anaesthetic:

Nearly all surgical procedures on hands should be carried out under anaesthetic. To "lance it in the office" too often means an inadequate stab as the patient jerks his hand away, like shooting at a moving target, and few of us are good enough for that. Infections are too painful to permit proper opening. The patient's failure to return does not mean that he is cured — he has gone to some one else.

a. *General Anaesthetic*: Often general anaesthesia is the only satisfactory one in spite of all the fuss which it necessitates for a mere "sore finger." There is no alternative for opening tendon sheaths or palmar spaces.

b. *Nerve Block*: For lesions limited to distal phalanx such as felon or paronychia, an alternative to general anaesthesia is offered in nerve block.

Injection of 1 cc. of 2% novocain around the digital nerve at each side of the base of the finger will give excellent anaesthesia for a short time. Skin must be carefully prepared because a clean surgical procedure is to be carried out fairly close to an infected area at the end of finger. Ten minutes must elapse before anaesthesia is established.

c. *Freezing*: Ethyl Chloride spray to freeze the skin is not good. It adds damage to already devitalized tissue. Accurate drainage is impossible. At best one must force the knife suddenly through a hard frozen crust. Furthermore, patients report that the freezing and thawing cause almost as much pain as to open the area without any anaesthetic.

d. *Local Infiltration*: Occasionally pus lies deep enough that the covering

skin is relatively normal. An "intradermal" weal may be raised with 2% novocain which gives instant anaesthesia for very short duration. The weal should be about ¼" wide, and knife cut can be made directly in the course of the weal. Infiltration of infected tissues is not good for fear of spreading cellulitis.

With the general principles well in mind, we may now discuss briefly their application to the more common type infections.

A—CELLULITIS.

The commonest and at the same time the most dangerous infection is caused by lodging of bacteria directly in the loose cellular tissues. Cellulitis ranges all the way from the thousands of sore fingers and small infections to the severe spreading streptococcal cellulitis with red streaks running up the arm. It is this latter with its lymphangitis and lymphadenitis which is dangerous and which is responsible for the occasional rapidly progressing and fatal case.

In all cellulitis, treatment must be extremely conservative. Rest in bed, hot wet dressings, electric cradle, fluids, and sedative, will enable patient to overcome most. To operate may satisfy the frantic relatives but will only facilitate the spread of infection and make patient worse. In fact, as Koch so graphically states: "In such cases if conservative measures do not bring about an arrest of the infectious process, one may be certain that surgical intervention will only hasten the inevitable and fatal outcome."

Localization and pus formation occurs only late in cellulitis and operation is indicated only when incontrovertible signs of pus are present. One is no longer dealing with cellulitis but with abscess, so the indications are different.

Prontylin is a new addition to the armament of the surgeon and has a place in any streptococcus infection. In some cases results are dramatic. Eighty grains per day should be given, and improvement should be evident in twenty-four hours if any is to be obtained.

B—TENDON SHEATH INFECTION.

Acute inflammation with pus formation in flexor tendon sheath is one of the most crippling types of infection that can befall a hand, for if the tendons are damaged the whole function of the hands, which is to grasp, is destroyed.

The diagnosis may be made by observing the four cardinal signs of acute tenosynovitis.

1. *History of injury*: Bacteria enter only through broken skin. A small puncture wound, a needle prick, a tack carries infection directly into sheath if the injury be over flexor creases where fat pad is lacking.

2. *Semi Flexion*: Inflammatory exudate increases pain because of increased tension. Semiflexion gives the most slack space and the most comfort.

3. *Tender over Sheath*: Inflammation quickly spreads to whole sheath. Pressure, therefore, will elicit tenderness which outlines the anatomical position of the sheath throughout its whole length, no matter where the original entry may have been. Thus is explained the tenderness in the distal part of palm.

4. *Tender on Movement*: Sliding of an inflamed tendon in an inflamed sheath causes pain just as respiration causes pain in pleurisy. Demonstrated by gently straightening the semi-flexed finger.

Immediate operation should follow the diagnosis of tenosynovitis in an effort to save the life of the tendon. Once death of tendon has occurred, good surgery can bring about subsidence of acute infection by drainage but cannot restore function to tendon.

Operation (see figure 1) must accomplish several details.

1. Drain sheath from end to end since it is infected from end to end. Nothing less is adequate.

2. Preserve digital nerves and vessels.

3. Prevent tendon from "bow stringing" out of its bed by leaving tiny bridges to hold it down.

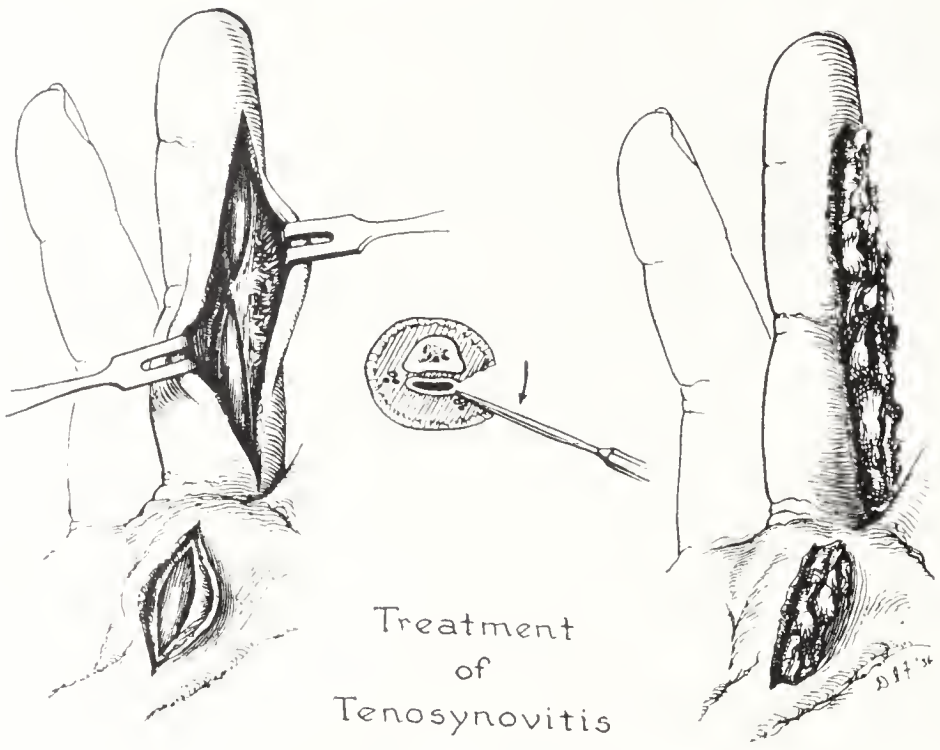

Figure 1.

4. Maintain drainage by loose packing.

C—FELON.

Acute inflammation in the anterior pulp space of the distal phalanx also demands immediate operation to avoid needless acute suffering for the patient and to avoid death of bone lying in a bed of pus.

Again the evidences which permit accurate diagnosis are small but clear.

1. *History of Injury*: A rose thorn, a needle, a "safety pin" used to fasten a dressing on an infected patient produce small injury in distal phalanx.

2. *Distal Phalanx*: In this case the process is limited to distal phalanx. the rest of the finger being normal.

3. *Tender*: Slight pressure over pulp of distal phalanx produces increase of the all ready severe pain. The tension which developes in this distal closed space is responsible for increased pain and tenderness.

4. *Swelling*: By comparing with the corresponding finger in the other hand the distal phalanx will be seen slightly swollen and definitely tense.

Operation (see figure 2) is carried out at once for the reasons stated above. Again it must be done thoroughly or not at all and must accomplish the following

1. Drain distal closed space from end to end and from side to side. Cut all the trabeculae across to ensure free flow.

2. Avoid stabbing bone with point of scalpel which has traversed infected field.

3. Avoid nicking end of tendon sheath for fear of adding tenosynovitis.

4. Maintain free flow by deep, loose packing.

D—PARONYCHIA.

Infection which finds its way into the soft tissue around base of nail is in a particularly bad place for adequate drainage to occur naturally. The space so involved extends from side to side, both above and below base of nail so that operation must be so designed to remove nail as well as open surface infection.

The typical picture is well known and is recognized by the following points:

1. *Distal phalanx*: Paronychia, like felon, is limited strictly to distal phalanx.. Rest of finger is normal and constitutional reaction is slight.

2. *Puffy*. The chief characteristic of lesion is the swollen, puffy red area just above the base of nail, extending across from side to side.

3. *Nail floating*: In late neglected cases, proximal part of nail is actually free from its bed and appears to be "floating" on a bed of pus, which can be seen through the nail.

Operation, if prompt and thorough will give patient comfort and get rid of infection in least possible time. The

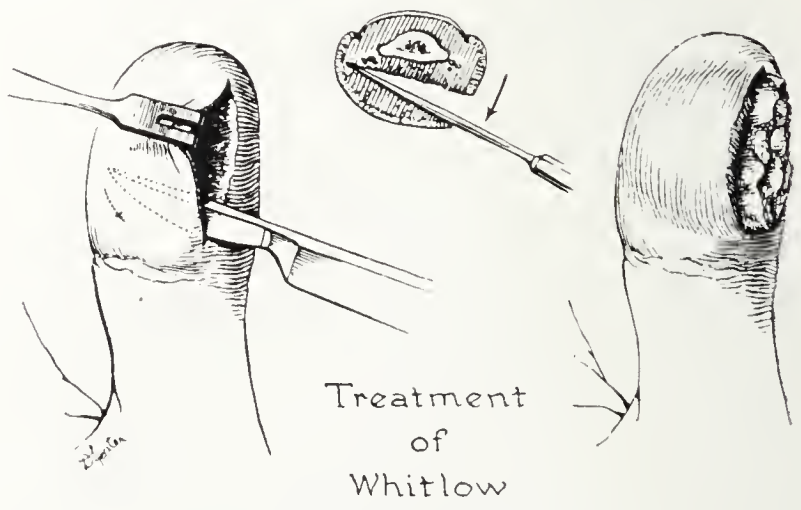

Figure 2.

details are shown in Figure 3 and are designed to accomplish the following steps:

1. Lift flap to drain space above base of nail.

2. Remove proximal half of nail to permit free drainage of space under nail.

3. Prevent flap from falling back and obstructing drainage.

The space devoted to clinical picture and description of operation is deliberately small because general principles are always more important and if clearly understood, can readily be applied to any specific problem. The drawings show clearly the steps of operation in each case.

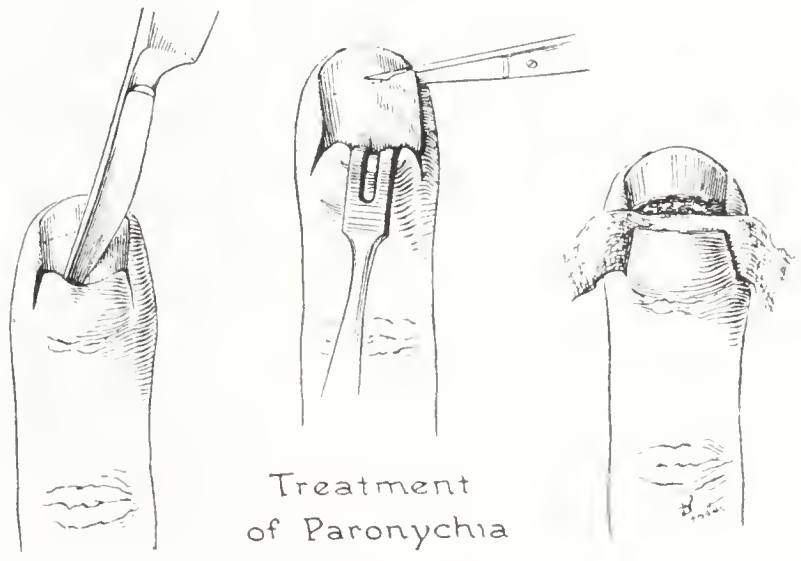

Figure 3.

REMARKS ON CHEMOTHERAPY

By P. H. GREEY, M.D.

Remarkable advances in chemotherapeutics have been made in recent years. The credit for this belongs entirely to Domagk and his associates, Mietzch and Klarer of the I. G. Farbenindustrie in Germany. The brilliant work and discoveries of Ehrlich, the father of chemotherapy, have thus been ably carried on by his fellow countrymen.

It is always instructive to know the steps and hypotheses that have led to scientific advances. Domagk's discovery apparently had its origin in the dyeing industry. It had been known for more than twenty years that certain chemical groups were necessary before azo dyes would be fast, without the use of mordants, for fabrics of plant origin. Someone suggested that such dyes might have a specific staining affinity for bacterial protoplasm and might themselves have a toxic action on the bacteria or be changed to a destructive compound through the addition of a toxiphore group. Domagk, acting on this suggestion, infected animals with a number of different pathogenic bacteria and treated them with all the dyes then available that possessed the fundamental chemical group conferring affinity for plant tissue. He found that animals survived a haemolytic streptococcal infection when they were treated with the substances now known as the prontosils. These substances he demonstrated had no harmful effect upon haemolytic streptococci and other bacteria in the test tube. This fact deserves special emphasis, for had Domagk carried out only the in vitro technique, which was then in common use, it is unlikely that the prontosils would have been discovered.

The mode of action of the prontosils, at first thought to be complex, was soon found to be relatively simple. Previous experience in chemotherapy had shown that even slight changes in the molecular structure of a specifically active compound rendered it inactive. It was, therefore, very surprising to find a number of different red dyes having similar activity. This suggested the presence of some group common to all the active compounds. It was later proved that the complex molecules of the prontosils became effective by reduction in the body to para-aminobenzenesulphonamide. This simpler compound, whose name is now abbreviated to sulphanilamide, was shown to

be of equal value in experimental infections and to have a bacteriostatic action on streptococci and other bacteria in the test tube. Sulphanilamide had been known as a chemical for many years, but its chemotherapeutic activity was not suspected. Heidelberger and Jacobs must have come very close to discovering its curative qualities when they worked with it in 1919.

Other Compounds.

The startling results obtained on treating certain human bacterial infections, first with the prontosils and later with sulphanilamide, awakened world-wide interest in chemotherapy. The result has been the synthesis of well over one thousand compounds with the object of improving on sulphanilamide through increasing therapeutic efficiency, reducing toxicity and finding compounds effective against bacteria that do not respond to sulphanilamide. The assessment of activity of these allied compounds has been made by experiments conducted in animals and in vitro. Only a few of the many have merited clinical trial, but even so the number of compounds available for clinical use is relatively large. One cannot but deplore the use of proprietary names for these new chemical agents. When one considers that sulphanilamide has been sold under at least forty different trade names, none of which have any chemical significance, and that even the same trade name has been applied to entirely different chemical substances some idea may be gained of the confusion that has been created by this procedure.

The world-wide search for improved chemical compounds has yielded at least one further forward step. This was announced last May by Whitby in England, when he reported that experimental pneumococcal infections in mice were cured by the administration of 2 (p - aminobenzenesulphonamido) - pyridine, first known as "May and Baker 693," later as Dagenan, more recently called sulfapyridine (a name equally lacking in chemical significance) by the Committee on Pharmacy and Chemistry, American Medical Association. The discovery of this new compound was obviously a great advance, for sulphanilamide does not possess significant curative powers in experimental pneumococcal infections. The pyridine derivative of it, however, produced just as spectacular results in experimental pneumococcus infections as sulphanilamide had in those due to haemolytic streptococci and was, therefore, submitted to clinical trial at once.

Some of the outstanding chemotherapeutic agents that have emerged from the intense investigations started by Domagk's announcement in 1935 are: (1) Prontosil, (2) Sulphanilamide, (3) Uleron, (4) Sulfapyridine, (5) Rodilone and (6) Promin. It would be impossible in the space available to consider in detail all of the information, experimental and clinical, that has accumulated in regard to these compounds in the past year or two. Advances are so rapid, publications so numerous, that most of what is written on chemotherapy is out of date before a journal can publish it. The following discussion, which has been gathered from the literature, will be confined, therefore, to sulphanilamide and "M & B 693."

Sulphanilamide

Sulphanilamide, which has been studied more extensively from all aspects than any of these compounds, forms the standard with which all new compounds have been compared. It is absorbed rapidly from the alimentary canal, soon reaches the blood and penetrates into all organs, secretions and effusions but at a somewhat lower concentration than exists in the blood. Excretion is by the urine and is usually complete in 48 hours. Approximately one half of the ingested dose is eventually conjugated in the liver to an acetylated compound which is therapeutically inactive. The rate of absorption varies considerably in different individuals as does conjugation and ex-

cretion; the latter may be much delayed by renal damage. The maximum blood concentrations do not persist for more than six hours and hence it is advisable to administer the drug at intervals of 4 hours. It is generally accepted that a blood concentration of about 10 mgm. per cent. should be attained in the seriously ill for the best therapeutic results. A total daily dose of 1 gram per 20 lbs. of body weight generally accomplishes this, but the amount to be administered can only be adequately controlled by determining the concentration of the drug in the blood by colorimetric means. This is an important adjunct to intelligent and successful therapy.

(1) *Streptococcal Infections.* Sulphanilamide is not a cure-all; it has been administered in a great many instances for diseases in which its use was not warranted. A bacteriological, as well as a clinical diagnosis must be made before sulphanilamide is used.

(a) *Haemolyticus.* The best experimental results have been obtained with haemolytic streptococci of Group A, and this is also true in the clinical field. Excellent clinical assessments have been made in *puerperal sepsis* due to haemolytic streptococci, in *erysipelas* and in streptococcal *meningitis.* In these sulphanilamide has produced dramatic results. It is also effective in *bacteraemia, cellulitis* and *lymphangitis.* These spreading infections probably depend primarily on the invasive qualities of the organism and sulphanilamide appears to depress this markedly. *Scarlet fever* per se is benefitted but little by sulphanilamide; the sequelae, due to the spread of the organism from the throat to adjacent structures, are reduced by drug therapy. Well developed *abscesses* do not respond well to sulphanilamide and should be drained. Not only does the abscess wall interfere with penetration but apparently the contained bacterial and cellular necrotic material diminishes the effectiveness of sulphanilamide. A similar absence of response has been noted also in lesions secondarily infected with Staphylococcus aureus.

Sulphanilamide does not usually eradicate the haemolytic streptococcus from mucous membranes, for it has been shown that cases of pharyngitis and puerperal sepsis still harbour the organism for long periods of time after the clinical signs of infection have subsided under sulphanilamide therapy.

(b) *Other Varieties.* While the growth of *Strep. viridans* is inhibited in vitro, by amounts of sulphanilamide attainable in the body the drug has proven ineffective in cases of *subacute bacterial endocarditis.* This may well be due to the pathological character of the lesion.

There is ample experimental and clinical data that *Strep. faecalis* does not respond to sulphanilamide. In the case of the *anaerobic streptococci* the evidence is not nearly so clear cut, but the indications are that such infections are not greatly benefitted by sulphanilamide.

(2) *Meningococcal Infections.* Here again the experimental and clinical assessment has been excellent. The drug alone has yielded better results than specific antiserum therapy alone in meningococcal meningitis. It has not been agreed upon as to what the optimum method of treatment should be: whether sulphanilamide should be given only by mouth or combined with the intrathecal route, whether alone or combined with specific antiserum. Experimentally serum and sulphanilamide have been found to be more effective than either alone.

(3) *Gonococcal Infections.* Probably more of the drug has been used in the treatment of *gonorrhoea* than of all other diseases combined. Claims of cure in as high as 95 per cent. of the treated cases have been made. Such claims, however, need to be critically considered in regard to the criteria used to determine cure. Indeed, it is now clear that a considerable number of patients may be rendered symptom-free by sulphanilamide and yet be dangerous through a residual latent infection, which can only be detected by special bacteriological

cultures. Most investigators have found that about 20 per cent. of the patients treated have failed to respond. Whether this depends upon strain differences in the gonococci or whether the method of sulphanilamide administration (which has been extremely variable) should be altered, has yet to be determined. There is considerable evidence that the best results are obtained when treatment is delayed until after the acute stage has passed. The drug is undoubtedly of great value in the treatment of gonorrhoea; under the best conditions of administration 45-70 per cent. of the cases are cured. It also greatly reduces the number of complications and is effective in *metastatic lesions*, in *ophthalmia* and in *epidemic vulvo-vaginitis*. It is questionable whether sulphanilamide has any value as a prophylactic.

Uleron, which is widely used in Germany and South Africa for gonococcal infections, is not in general use in this country because of the occasional occurrence of polyneuritis (foot-drop).

(4) *Urinary Tract Infections.* Successful therapy of the preceding diseases has depended upon the attainment of an adequate concentration of sulphanilamide in the blood and tissue fluids, because the bacteria are interstititial fluid parasites. The danger of toxicity is great if the blood concentration of sulphanilamide is raised above 15 mgm. per cent. This of necessity limits the action of sulphanilamide to bacteria that are readily susceptible. The situation in urinary tract infections is very different for as has been mentioned above, the drug is excreted by the kidney and therefore appears in the urine in high concentrations (up to twenty times that in the blood). This permits a range of action on bacteria that are not affected by concentrations attainable elsewhere in the body.

Non-specific urinary tract infections due to such organisms as *B. coli*, *B. proteus, B. lactis aerogenes* and *Staphylococcus aureus and albus* respond quickly to sulphanilamide therapy provided that the infection is not complicated by stone, tumour or malformation. If such be present the response is not nearly as good. Furthermore, the doses of drug administered can be relatively small. Sulphanilamide, however, has no effect upon urinary tract infections due to *Strep. faecalis* and *Group D haemolytic streptococci.*

(5) *Miscellaneous Infections.* Successes have been claimed in *staphylococcal, typhoid and paratyphoid infections,* in *gas gangrene,undulant fever, malaria, bubonic plague, trachoma, actinomycosis* and *lymphogranuloma inguinale.* It is difficult to evaluate the effectiveness of sulphanilamide in these as many would have recovered spontaneously, and final judgment cannot be passed until an organized clinical assessment has been made in each condition. It is of interest to note that the first human case successfully treated with prontosil was one of generalized staphylococcal infection.

Experimentally the *viruses* of poliomyelitis, herpes, encephalitis and influenza have not been affected by sulphanilamide. The reported successful treatment of canine distemper with sodium sulphanilyl-sulphanilate has not been confirmed. Negative results have been obtained in experimental syphilis, in avian malaria and with trypanosomes in mice.

Some successes have been recorded in *pneumococcal* pneumonia and meningitis The scarcity of clinical reports, coupled with the rather poor results obtained experimentally, indicate that sulphanilamide has little effect on the pneumococcus.

"May & Baker 693" (Sulfapyridine)

Experimentally Whitby has shown that while the range of activity of "693" includes the pneumococcus, this broadening of chemotherapeutic action is not associated with any loss of effectiveness against the haemolytic streptococcus. Although it is but eight months since the discovery of this compound was announced much already has been learned about it.

The absorption, conjugation and excretion have been studied and the drug has been found to behave in much the same way as sulphanilamide in the body. Toxic manifestations are similar to and about as frequent as those with sulphanilamide.

The drug is at present receiving thorough clinical trial. From the data available, its effect in *pneumococcal pneumonia* is but little short of miraculous. Only small series have so far been reported but in these the mortality rate in those treated has been about 8 per cent both in England and the U.S.A. Professor Graham recently reported to the Toronto Academy of Medicine the first adequately controlled alternate-case series. He found from his controls that the pneumonia mortality in Toronto this season was of average severity with a rate of about 25 per cent. In marked contrast to this stood the cases treated with "M & B 693," in whom the rate was only 6.5 per cent. Present indications are that "M & B 693" will be one of the greatest advances so far made in the treatment of pneumococcal pneumonia.

Several reports of recovery from *pneumococcal meningitis* by "M & B 693" have appeared. These dramatic recoveries are reminiscent of the early days of sulphanilamide therapy when recovery, through chemical treatment, from meningitis due to Strep. haemolyticus did more than anything else to focus the attention of the medical profession on the new chemotherapeutic agents.

Mode of Action.

This aspect of the subject has received the attention of many research workers. If it were clearly understood how these compounds act it would then be possible from the theoretical side to forecast activity and perhaps to devise some method of preliminary trial for new preparations less laborious than the present evaluation in experimental infections.

Three main hypotheses have been advanced; one that the drugs exert a bacteriostatic or bactericidal action on the invading organism; another, that they have a detoxicating action, neutralizing bacterial toxic products; and the third possibility is a stimulation of phagocytic activity. While the data in favour of the latter two is meagre, we have ample evidence that sulphanilamide exerts a bacteriostatic action which becomes bactericidal under certain conditions. This slowing down of bacterial multiplication is considered to be sufficiently marked to allow the natural body defences to eliminate the infecting bacteria. However, this hypothesis, which is the one most widely accepted may not be the full explanation as other possibilities have still to be investigated.

The mode of action of "M & B 693" on the pneumococcus has been but little studied. The work done, however, tends to show that its action is a more direct one than sulphanilamide, and that it is definitely more bactericidal. Furthermore, it has been stated that "M & B 693" affects the protective capsule of the pneumococcus, eventually destroying it altogether. If this observation is adequately confirmed it will afford a satisfactory explanation of the curative powers of the drug.

BENZEDRINE SULPHATE

By J. K. W. FERGUSON,
Department of Pharmacology

Benzedrine in the form of the volatile alkaloid has been used for several years as an inhalant to shrink the nasal mucous membranes. It has enjoyed considerable popularity in spite of an unfortunate tendency to produce sleeplessness. The potential value of this annoying side effect was not realized till Prinzmetal and Bloomberg (1935) turned the nuisance neatly to advantage in the treatment of narcolepsy. They gave benzedrine sulphate by mouth. It worked so well in combatting the mental depression and somnolence of the narcolepsies, that there was an immediate rush to try it in every ailment that might possibly be helped by a central stimulant. Dozens of papers have since appeared, describing its effects in such diverse conditions as dementia praecox, depressive psychoses, anxiety states, Parkinsonian syndromes, pylorospasm, obesity, and the performance of school work. That the drug will hold a place in the doctor's armamentarium seems certain. It is, however, too soon to set with any confidence the limits of its usefulness, but it does seem that the condition most consistently benefited is narcolepsy. It should be noted that undesirable and even dangerous effects on both ill and healthy persons have also been obtained, and all writers agree that benzedrine sulphate, like any other potent drug, must be used with care.

Benzedrine is related chemically to epinephrine and has many similar actions. It is of somewhat simpler structure than epinephrine, having no hydroxyl groups in the molecule. It may be described as racemic beta-phenyl-isopropylamine, with the formula $C_6H_5\text{-}CH_2\text{-}CH(NH_2)\text{-}CH_3$. It has been accepted for several years by the Council on Pharmacy and Chemistry of the A.M.A. as active ingredient in an inhalant or nasal spray. Benzedrine sulphate for oral administration, however, was accepted only in time to appear in the supplement to New and Non-Official Remedies of 1938, where its actions and uses are concisely described.

The one outstanding and practically invariable result of an effective dose (5-20 mg.) of benzedrine sulphate is sleeplessness. The psychic accompaniments of this action are apparently very variable. This is of course only to be expected of a drug which works at levels of the nervous system where individual variations in function are most prominent. Several writers have painted highly attractive pictures of the psychic actions. These are alleged to include a sense of exhilaration and self-confidence resembling an alcoholic euphoria with some added advantages. It is said that the performance of mental tests is not impaired and may even be improved. In this connection some tests (by Bradley) on thirty children are of interest. Under the influence of the drug about half the children seemed subdued; the other half elated. About one half showed a definite improvement in their school work, but the improved performance seemed to be quite independent of whether the child was elated or subdued.

It is not surprising that the more glowing accounts of the actions of benzedrine sulphate quickly attracted the attention of the popular press. The word soon passed around that a new thrill was available. Students were quick to appreciate a new aid in the old game of burning the candle at both ends. College authorities regarded the situation with well founded alarm. Fortunately it does not seem likely that the worst fear, namely that widespread addiction to the drug

might develop, will be realized, for the simple reason that to the great majority of people the effects of the drug are not attractive. In a carefully controlled test on some hundred and fifty medical students, Gwynn and Yater found that the great majority expressed no desire to use the drug again. A number (30) felt that they might want to use it temporarily in certain contingencies. Only a few (8) expressed any desire to continue its use. Many patients have now been receiving the drug for several years and so far no case of true addiction has been reported. That is to say, withdrawal of the drug produces no symptoms comparable to the agonizing withdrawal symptoms of the morphine addict. Furthermore, no tendency to require larger and larger doses has been observed.

It appears then that to most normal people the drug will not be attractive. The sensation it often produces may be described as a tremulous restlessness. To those who find the drug attractive, a strong warning must be issued. There is no doubt that the drug can obscure the signs and sensations of normal fatigue. Prolonged use for this purpose is obviously courting a mental or physical breakdown. A brief report from the Netherlands indicates that four medical students have developed more or less serious neuroses following prolonged use of the drug.

Experiences with the drug which have been reported to date, suggest certain conditions in which unfavourable effects may be expected. According to Anderson, depressed patients may be aroused from an apathetic state only enough to make active attempts at suicide. Pugnacious and homicidal tendencies may also be accentuated and make the use of the drug hazardous if adequate control and observation of the patient are not secured. It seems, too, that patients with cardiovascular disease, and the elderly, are not fit subjects for the drug, since therapeutic doses of the drug will often, though not always, increase the heart rate and blood pressure. One case of severe aplastic anaemia following the use of benzedrine sulphate has been reported. This, however, may be coincidental. Loss of appetite has been reported frequently. In one case this lasted for several months after the drug had been discontinued.

Enough evidence has accumulated regarding the dangerous potentialities of benzedrine that in Great Britain it has been placed on the schedule of drugs which may be sold only on a doctor's prescription. Doubtless there will be agitation to have its sale similarly restricted here. So far as the writer can tell from his inquiries of pharmacists and medical practitioners there is little evidence that benzedrine is being misused in Toronto. It is hoped that medical students will use their discretion and influence to maintain this situation.

REFERENCES.

Prinzmetal, M., and Bloomberg, W.—1935. J.A.M.A. 105. 2051.

Anderson, E. W.—1938. Brit. Med. J. July 9.

Bradley, C.—1937. Am. J. Psychiat. 94. 577.

Gwynn, H. B., and Yater, W. M.—1937. Med. Ann. D. of Columb. 6. 356.

Davies, I. J.—1937. Brit. Med. J. Sept. 25. 615. (Review of toxic effects).

SOME FAMOUS MEDICAL SCHOOLS

THE JOHNS HOPKINS HOSPITAL AND MEDICAL SCHOOL

By F. T. LAROCHELLE

The Johns Hopkins Hospital, though governed by its own group of trustees, and endowed independently of the Medical School, is so closely related to the School of Medicine that it would be quite impossible to consider them in any other fashion than as a functional unit. Indeed, it was directed in the will of the founder that the Medical School, upon its erection, should become a part of the Hospital. The Director of the Hospital and the heads of its main departments serve on the faculty of the School of Medicine.

The Johns Hopkins Hospital was incorporated in 1867, and the Trustees of the University and Hospital were organized three years later. At his death in 1873, Johns Hopkins, a Baltimore merchant and banker, bequeathed the greater part of his fortune for the organization of a university and hospital. The planning and execution of the project he wisely delegated to his board of trustees. His only stipulations were that the fund be made as productive as possible, and that further, the hospital should be for the benefit of the indigent sick of Baltimore and its environs "without regard to sex, age, or color;" that a training school for nurses be established in conjunction with the hospital, as well as dispensary accomodations; that the hospital should be free of any sectarian influences; and that it should ultimately form part of the medical school of the University, and thus further the cause of scientific research and medical education. In these instructions to the Trustees it was stated that the plan should "provide for a hospital which shall, in structure and arrangement compare favorably with any other institution of like character in this country, or in Europe."

In the fall of 1874 the Board of Trustees offered to President Daniel Coit Gilman of the University of California, the first presidency of the Johns Hopkins University. From those early days until his retirement in 1901, President Gilman "manifested the greatest wisdom and foresight and did the best

possible service to the future school of medicine." Early in the history of the University he brought together a nucleus of distinguished physicians who were a few years later to constitute the faculty of the Medical School. The achievement of a medical school on the basis of a higher university was largely the work of President Gilman and will be remembered as one of the greatest achievements in the cause of higher education.

A year and a half after the death of Johns Hopkins, the Trustees accepted the plans submitted by Dr. John Shaw Billings for the construction of the hospital. These plans were not used in the original form. For two years Dr. Billings traveled through this country and Europe diligently studying hospital construction before a final set of plans were drawn up for use. Construction was begun in 1877 and the Hospital was formally opened in 1889.

Largely through the generosity of a number of Baltimore women, of whom Miss Mary E. Garrett was the principal donor, the School of Medicine was opened in the fall of 1893.

Between the founding of the Hospital and the opening of the Medical School a distinguished group of men was selected to constitute the faculty of the new school. The earliest of these appointments was that of Professor William H. Welsh to the chair of pathology in 1884. In 1888 Dr. William Osler was elected Physician-in-chief to the Hospital. These were followed by the appointments of Professor William S. Halsted to the chair of surgery, Professor Howard A. Kelly to the chair of gynecology, Professor William S. Thayer in internal medicine, Professor J. Whitredge Williams in obstetrics, and Professor Henry M. Thomas in neurology. Around these were grouped a cluster of younger men: Lewellys F. Barker, Simon Flexnor, W. T. Councilman, H. A. Lafleur, Charles P. Emerson, A. C. Abbott, Thomas S. Cullen, and others. With this nucleus as a faculty, medical teaching began.

By 1894 the Medical School was in full swing. Recognition came quickly and before many years the new school and hospital had established Baltimore as one of the great medical centres of the world. Growth has been equally rapid. The Hospital at present has a capacity of 919 beds, and is composed of a group of buildings occupying a whole city block and parts of two others. In addition to the administration building, the Dispensary, and two nurses' homes, there is the Marburg building for private patients, the William Holland Wilmer Ophthalmological Institute, the Harriet Lane Home for Invalid Children, the Henry Phipps Psychiatric Clinic, the James Buchanan Brady Urological Institute, the Halsted Surgical Clinic, the Osler Medical Clinic, and the Woman's Clinic. The Medical School and William H. Welch Medical Library are contained in an adjacent block, and in still another block, located directly across from the Woman's Clinic, is the School of Hygiene and Public Health.

The latest addition to the Hospital and Medical School has been the Welch Memorial Library, opened in 1929. Its collections formerly comprised the Hospital Library, the library of the Medical School, and the library of the School of Hygiene. It contains approximately 116,000 volumes. The library of the Medical and Chirurgical Faculty of Maryland located nearby to the Medical School contains 60,000 volumes. The University Library containing 387,437 volumes, as well as the Peabody Library and the Enoch Pratt Library containing 248,000 and 716,000 volumes respectively are open to students of medicine. Washington is so near that its libraries and museums are easily accessible to the student. Among those of interest are the Smithsonian Institution and National Museum, the Library of Congress, the library of the Surgeon-General's office,

and the libraries of the various departments and bureaus.

The curricular activities of the medical school are arranged with regard for the so-called concentration system devised by Dr. Franklin P. Mall, formerly professor of anatomy at the Medical School. When first formulated, the system was intended to apply only to those subjects taught in the first two years, that is to say, to the pre-clinical sciences, but in a general way it has been spread throughout the entire medical course. Dr. Mall proposed that only two subjects be taught at one time, and that they should be taught intensively.

During the first two quarters of the first year, the student spends his entire time in anatomy and histology, devoting four hours each morning to the former and three hours, three afternoons a week to the latter. The two remaining afternoons of the week are left free for the student to use in elective work, or in whatever other manner he wishes. Properly qualified students, even as early as the first year, are allowed to take part in research, either in one of the various laboratories of the Medical School, or in the case of a select few, in the Carnegie Institute, an institution for biological and medical research, located on the grounds of the Medical School. During the third and fourth quarters of the first year the student devotes the most of his time to physiology, physiological chemistry, and neurology with concentrated instruction in each.

At the beginning of the second year the student moves "across the street," as it is called, to the department of pathology and bacteriology, where for three quarters his time is largely taken up by intensive instruction in morphological aspects of diseased tissue. Instruction in pathology resolves itself into five phases. For one hour each morning a lecture by a member of the staff is heard by the entire class. In addition to this, the class as a whole attends the Clinical-Pathological Conferences held for one hour, two days a week. These conferences are chiefly for the benefit of the upper classes, but they afford the second year student an opportunity to introduce himself to clinical findings, and at the same time to correlate the signs and symptoms with the pattern of pathologic changes observed. The class also meets as a whole at a weekly "organ recital" at which time gross pathological specimens of particular interest are demonstrated by a member of the staff. Except for the morning lecture and these other occasional meetings, the class is divided into groups of approximately ten students and to each group is assigned three instructors. These groups work as units. The gross material is arranged in rooms; all the specimens illustrating one disease or a class of diseases are placed in a single room. The groups circulate through these rooms spending from a week to two weeks in each, according to the complexity of the subject being studied. For study during the part of each day not spent in attending the lectures and studying gross material, each student is provided with a set of slides illustrating pathologic changes to be observed microscopically. In this study he is guided by the instructors assigned to his group. In addition to these items of instruction, each group is encouraged to witness and assist in autopsies performed by its instructors, and on occasion, by instructors of other groups.

The last part of the second year is occupied by a series of courses designed to prepare the student to take part in the activities of the clinic during his third year.

The third year is devoted to concentrated instruction in medicine, surgery, obstetrics, and psychiatry and neurology, each for a quarter, and to attendance at the various clinics.

The instruction during the fourth year comprises only half of the allotted time, consisting of one quarter each in medicine and surgery. During the remainder of the time the student is

allowed to follow any one of a number of courses; he may take elective work or spend his time in research; or if he wishes, he may migrate to other institutions either in this country or abroad.

Throughout the course of medicine there is a basic minimum prescribed for all students, but above and beyond this minimum the student's energy is the only restriction upon his activities. One of the fundamental ideals of the University is freedom of study, and this is amply reflected in the outline of the course of study set up for the students of medicine.

There is another curricular arrangement that is unique, and therefore, worthy of mention. In the medical course psychiatry is a required subject, and must be taken at least during one quarter of each of the four years. In the first year the student attends a course of lectures delivered by Dr. Adolph Meyer upon the subject of psychobiology, and in conjunction with this, writes a summary of his own life activity in order that he will have an opportunity to study the quality of the psychobiologic activity in the normal individual before attempting to study individuals in whom the psychobiologic complex has undergone alteration. This is followed during the second year by a course of lectures on the principles of psychiatry and practical instruction in examining patients. During the third year one quarter is devoted to psychiatry, and during the fourth year, the student attends the psychiatric clinic. Ample opportunity is given for elective work and for research.

The percentage system of marking students has been abandoned in the Medical School. Examinations, with few exceptions, come only at the end of the school year, at which time the student is given an oral and written examination by the instructors in the required courses taken during the year. No examinations are given in elective work.

During the medical course most of the instruction is given at the Johns Hopkins Hospital, but the facilities of the various departments of the city and state hospitals are utilized for a portion of the clinical instruction.

Students enrolled in the Medical School are drawn from all parts of this country and many foreign lands. Among the members of the present senior class are representatives of 25 states and 3 foreign countries. Each class is limited to approximately seventy-five students. Those places in each class that for some reason become vacated, are filled by transfers from other schools.

There is ample opportunty for graduate study offered in the various departments. These graduates assist in the care of out-patients, do a certain amount of laboratory work, and occasionally undertake an investigation in the clinics or the laboratories.

The student is encouraged to take an active part in the various societies and clubs associated with the Hospital and Medical School. The Johns Hopkins Medical Society meets once a month; there are a number of departmental journal clubs, and the Baltimore City Medical Society meets regularly. Once every month during the academic year, there is a meeting of the Medical History Club. Since its founding, shortly after the opening of the Hospital, the members of the faculty and the students have taken an active interest in this organization. This interest was directly responsible for the founding, in 1929, of an independent Institute for the History of Medicine, conveniently located on the third floor of the Medical Library.

During the late nineties, Max Broedel was brought from Leipzig to Johns Hopkins, and here established the Institute of Art as applied to Medicine. Here the student may obtain instruction in medical illustration. The Institution has its own classes and its own groups of students, but special classes are given each fall for students of medicine. The School of Hygiene and Public Health was opened

in 1918 and in 1925 moved into its present quarters. All courses in the School of Hygiene are open to students of medicine without payment of additional fees, if the student obtains the consent of the instructor giving the course. Such courses may be taken as elective work.

Each year a certain number from the graduating class are appointed Resident House Officers in the various services of the Johns Hopkins Hospital. Other members accept internships in hospitals located in or about Baltimore, and the remaining group receive internships in hospitals located throughout the country.

The founding of Johns Hopkins was a milestone. It came at a time when American medicine was at a low ebb, falling prey to the malignancy of commercialism. It was destined to raise American medicine in the short space of fifty years to levels reached in Europe only after centuries of effort. It marked the establishment not of a mere school, nor of a hospital, but indeed, the beginning of American medical research that was rapidly to become the centre of gravity of the medical research of the world. This was the work of brilliant men who toiled with unceasing effort toward a great ideal. Space permits recounting the names of only a few of those who worked here, and by their work aided in the vitalization of American medicine. Welch, Osler, Kelly, Halsted, Thayer, Williams, Thomas, Barker, Councilman, Simon Flexnor, Cullen, Emerson, Abbott, Mall, Lafleur, Wright, Sternberg, Walter Reed, Carroll, Lazear, Gilchrist, Schenck, Cushing, Crowe, Rowntree, Geraghty, Abel, Howell, MacCallum, Opie, and many others; they will be remembered as great contributors to the cause of American medical progress. The Johns Hopkins has maintained its high place among medical institutions; its graduates continue to carry the spirit of its teaching all over the United States.

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The Examination for the Fellowship is divided into two parts viz., the first examination, or Primary, and the second examination, or Final.

The subjects of the Primary Examination are:—

Anatomy, including Histology and Embryology.
Physiology, including Biochemistry.

The Primary Examination is partly written and partly oral and must be passed as a whole.

The Primary Examination may be taken at any time after the candidate has completed a course of study and passed the examinations in Anatomy, Histology, Embryology, Physiology and Biochemistry in a Medical School or University approved by Council. The candidate must submit a certificate thereof with his application.

LANGUAGES OF EXAMINATION

Candidates at the time of making application for either the Primary or the Final Examination shall indicate whether they desire to be examined in the French or English language. Application forms printed in either language may be obtained.

STANDARDS OF QUALIFICATION

No particular list of text books or syllabus is recommended to cover any subject.

All candidates are expected to demonstrate a thorough knowledge of the subjects in which they are to be examined and, in the Final Examination, to be familiar with the current literature relating thereto.

PLACES AND DATES OF EXAMINATIONS, 1939

The Primary and Final Examinations will be held in the month of October.

The Written examinations will be conducted in eight or more centres in Canada on October 2nd, 3rd and 4th.

The centres selected to date are Vancouver, Edmonton, Saskatoon, Winnipeg, Toronto, Montreal, Quebec, Halifax.

If successful in the Written examinations candidates will be notified to assemble at the centres for Oral and Clinical Examinations viz—Halifax and Toronto for English speaking candidates, and Montreal or Quebec for French speaking candidates.

A Special Examination in the Primary subjects for English speaking candidates will be held in Montreal in June 1939.

The entire examination, written and oral will be held in Montreal with an interval of only a few days.

Dates — Writtens, June 12 and 13. Orals, June 19 and 20.

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WATER BALANCE AND ITS RELATION TO SURGICAL CONDITIONS

PART I.

By G. A. LANE, '40

The importance of water balance in both medicine and surgery is rapidly gaining a well-deserved prominence. Water, while not as necessary to the body as oxygen, is even more necessary than food. The physiological processes by which life itself is maintained, are only made possible because of the presence, and the properties of this simple fluid. In health, the water exchange is adequately controlled by the appetites; but in disease, all too often, it must be determined by the medical attendant. It is not enough to say — "This patient needs fluids. Let us give him an intravenous, it can't hurt him anyway." On the contrary it can and, all too often, does hurt him. If such shotgun therapy is to be avoided it is absolutely essential that student and practitioner have a working knowledge of the principles of water balance. It is in an attempt to clarify these principles, and to emphasize their importance, that this paper is presented. In this portion, there will be presented a brief review of the physiology of Water Balance. and, in a general way, the clinical application of this knowledge.

A—Normal Water Exchange

I.—Water Content of the Body; and its Distribution.
1. Plasma
2. Intercellular Fluid
3. Intracellular Fluid

II.—Water Balance of the Body.
1. External Fluid Balance
2. Internal Fluid Balance
3. Salt Metabolism

B—Abnormal Water Exchange

I.—Water Intoxication
II.—Oedema
III.—Dehydration

C— Conclusion.

A — Normal Water Exchange

I.—The water content of the body amounts to 63% of the total body weight. It is stored in varying amounts in the different tissues, but can conveniently be divided into three great fluid compartments.

1.—*The Blood Plasma.* Although this vascular compartment is the smallest of the three, it is in many respects the most important, since it forms the essential link between the external and internal environments of the body. While this compartment amounts to only 5% of the body weight, or about 3 Litres, it is kept remarkably constant in the healthy individual. Minor variations in level occur physiologically with such factors as a change in temperature, posture, or exercise, but the organism as a whole is so tuned that any gross disturbance is at once neutralized by an appropriate change in the internal fluid balance.

2.—Next we come to the *interstitial fluid.* This compartment contains 15% of the body weight, or some 9 Litres. It forms the great reservoir of body water, which sustains the plasma volume. It acts as an osmotic buffer, a large, homogeneous mass of water and salts, with no internal restraint other than that imposed by the endothelial membranes. Under the combined forces of the hydrostatic and osmotic pressures, it can be rapidly moved and aggregated where needed. It may undergo temporary changes in volume and osmotic pressures, but by means of the blood and lymph, it is as it were, rapidly stirred, so that disturbances are speedily distributed over the whole mass of fluid.

3.—Lastly, there is the *intracellular compartment,* amounting to 50% of the body weight, or about 30 Litres. As

the fluid in this compartment is essential for the health of the cells, the body processes are adjusted so as to keep this compartment intact. The cells, protected by their impervious walls, undergo only minimal changes. While there may be slight variations in their contents, these variations are small and transitory, as they are distributed over the whole cell mass of the body and are rapidly adjusted by the excretory organs. That this protection is adequate, is shown by the fact that those organs which consist mainly of parenchyma, show little loss of water, even in severe dehydration.

II.—WATER BALANCE OF THE BODY

I.—The external fluid balance depends on two factors — the ratio of fluid intake and output; and the total electrolyte content of the body. The latter factor will be discussed under salt metabolism.

The ultimate source of body water is from the fluid taken in, either preformed, or as the elementary constituents. (1) The most obvious source is water ingested as such. The amount taken varies from day to day with conditions such as heat, humidity, and exercise; but normally the range is from 800 to 2000 c.c.'s per 24 hrs. (2) In addition to this source, large amounts of water are taken in with food. Even so-called "solid" foods consist of 80% water. (3) Over and above this intake, however, food material provides another source of water, nearly as great, when it undergoes oxidation in the body.

Rountree has estimated that in the metabolism of 100 grams of fat, carbohydrate and protein respectively 107; 55; and 41 grams of water are yielded. Roughly the water content of the food, plus the water of oxidation amounts to 9/10th of its weight. In this manner, the usual hospital menu furnishes about 1200 c.c.'s of water a day. The soft diet furnishes about 500 c.c's.

Normally there is no other factor concerned in water intake; but it must be remembered that when weight is either lost or gained;—that is when food is either being stored in the body or removed; water is also either deposited in the tissues or is made available for use by the body. While fat is stored relatively free from fluid, 3 grams of water are deposited for each gram of glycogen or of protein. Whenever body materials themselves are burned, as in starvation, varying amounts of water are liberated. Totalling these various sources of fluid, the average daily intake is found to be in the neighbourhood of 3 litres.

While all water is taken in through the one channel, there are several modes of exit. (1) First we have the insensible cutaneous evaporation. This is very important surgically because it is insensible. This process is part of the mechanism for the control of body temperature, and under comfortable environmental conditions, involves the loss of 1000 to 1500 c.c's daily. The importance of this loss lies in the fact that it is continuous, it involves large amounts of water, and finally under many surgical conditions, the loss from this source may be tremendously increased. It must be emphasized that the water used in this manner has preferential rights; that is the body will vaporize fluid to control body temperature at the expense of water needed for excretion by the kidney.

(2) Water is also vaporized by the lungs. Expired air is saturated to the extent of 98% and so carries away fluid amounting under basal conditions to 300 c.c's per 24 hrs. This increases with any condition causing an increase in respiration.

(3) The sweat glands are inactive under basal conditions and function mainly as an emergency mechanism for heat loss during exercise or exposure to high environmental temperature. This loss is not negligible, however, as under certain conditions 8-10 Litres daily have been lost by this route.

(4) A certain amount of water is excreted in the feces. Some of this has

never undergone absorption; some has been secreted in the digestive juices; and some has been excreted in the colon along with substances such as calcium, or sulphate. Normally the loss in this manner rarely exceeds 200 c.c's daily.

(5) Small amounts of water are lost regularly in secretions such as the tears and saliva. Usually these losses are of no importance, but under certain conditions they may be greatly increased and then must be included in any calculation of water balance.

(6) Abnormal losses of fluid such as in hemorrhage, vomiting, or diarrhea, must also be borne in mind. The importance of any loss of gastro-intestinal secretions becomes more obvious if it is remembered that the daily secretion of digestive juices amounts to 7 or 8 litres, a volume over twice as great as the total blood plasma. Normally this large amount of fluid is reabsorbed as part of the intermediate water exchange, but abnormally, the loss from this source may be tremendous.

(7) Last of all the channels of excretion, I have placed the urinary system, because that is where it seems to come. Important as is the excretion of urine, the kidneys can only avail themselves of the water left after the other channels have been satisfied. While there is a minimal requirement, the normal kidney can handle any excess water that may be ingested. The kidneys thus form the spillway by which normal water balance is maintained. On the average one c.c. of urine is excreted per minute, or roughly 1500 c.c's per day. This daily excretion contains 35 grams of waste products. The minimum fluid requirement for adequate excretory function is determined by the ceiling of renal concentrating power. A normal kidney which can concentrate to a specific gravity of 1035 requires an output of 500 c.c's urine. A damaged kidney which can only concentrate to a specific gravity of 1015, requires 1500 c.c's. Below these amounts, there is retention and disturbance of acid-base balance; above them, function is normal. Hence in the treatment of negative water balance, a urinary excretion of 1500 c.c's is a desideratum.

II.—Returning now to the second aspect of this problem we will briefly deal with the subject of *internal fluid balance.*

(1) The exchange between the plasma and interstitial compartments largely depends on the resultant of the forces of hydrostatic and osmotic pressure exerted by these fluids. Separating the two compartments is a semi-permeable membrane, the capillary wall. Tending to force fluid out is the hydrostatic pressure of the blood in the capillaries assisted by the minor effect of any exuded plasma colloid. Opposing this tendency is the osmotic attraction exerted by the plasma proteins together with the effect of the tissue hydrostatic pressure. Under physiological conditions, the electrolytes take no part in this balance, as the capillary wall is freely permeable to them; and consequently the interstitial fluid has practically the same composition as protein-free plasma. As a result of variations in these forces, there is a minor circulation of fluid from the capillaries to the tissue fluid and back. There is another factor in this balance, in that any exuded protein cannot return directly to the capillaries, but must travel round to the back door by way of the lymph stream. Numerous physiological factors will cause variations in these forces and a temporary disruption of the balance.

(2) The mechanism regulating the exchange between the intracellular and interstitial compartments is somewhat different. Here the dividing membrane is impermeable to electrolytes. On the one hand we have the osmotic pressure of the sodium salts found in the tissues, and on the other is the balancing force exerted by the potassium salts and the proteins occurring in the cells. The turgor pressure of the cell and the hydrostatic pres-

sure of the tissue fluid, play but little part. Any alterations in the two forces are adjusted, not by a shift of electrolytes, but rather by a shift of water. Physiologically, however, only small variations occur as it is necessary for the health of the cell, that its content of fluid, be kept intact.

III.—In reviewing the physiology of water balance, the final factor that must be discussed, is that of *salt metabolism*. In addition to its important role in the maintenance of acid-base balance, sodium chloride, through its influence on osmotic pressure, helps to regulate the amount and distribution of body water. The total amount of water that the body can retain and the distribution of that water depends largely if not entirely upon the total electrolytic composition of the body fluids. Gamble and Ross have pointed out that when the chloride ion is lost from the body, it is easily replaced by the bicarbonate ion which is readily formed from carbonic acid. Thus the total electrolyte content of the body remains the same and there is no significant change in electrolytes or in body water. However, when sodium is lost, no other ion can adequately take its place and in order to maintain the acid base balance of the body bicarbonate and chloride ions are excreted. Thus there is a definite depletion of total electrolyte and this in turn leads to a decrease in body water. Thus it seems that the removal of sodium ions is the essential factor in the dehydration so commonly associated with loss of gastro-intestinal secretions, and other body fluids.

The normal sodium chloride concentration in the blood plasma ranges from 560 to 630 mgms. /100 c.c's. Thus level is maintained by the dietary intake, and by the efficient regulatory mechanism of the kidneys. Between 6 and 8 grams of salt are ingested daily. Of this half a gram is lost in feces and sweat, and the rest, if not used by the body, is excreted in the urine. If the intake is excessive this surplus is also rapidly excreted in the urine, with any available water. In many sick patients on the contrary, much of this excess salt is retained in the interstitial spaces, and edema may develop. This is particularly liable to occur from the indiscriminant use of normal saline for intravenous administration. A deficient salt intake rapidly causes an increased efficiency in the conservation of body salt. The same process occurs if there is an abnormal loss of salt. In spite of this protective mechanism, however, derangements of body function, and eventually dehydration do occur.

B — Abnormal Water Exchange

An attempt has been made to review briefly the physiological aspect of water balance. The clinical application of this is very important, both from the point of view of disturbances that occur in surgical conditions, and disturbances that are induced by the attendant due to an inadequate grasp of these principles. An upset in water balance may consist of an undue accumulation or a decreased content of water in the body.

I.—Undue accumulation of water in the body leads, not to the condition of edema, but to a less well known condition, that of *water intoxication*. The subject of water intoxication has attracted but little attention, but, mild forms of the condition may be commoner than is realized. It never occurs under natural circumstances as the water intake is limited by nature. Pathologically it occurs whenever water is retained by the body, without an equivalent amount of salt. The essential feature of the condition is not the total amount of water retained, but the accumulation of water in the body out of proportion to the sodium chloride content. That this is true can be seen from the fact that in a condition such as miner's cramp, where large amounts of water, and salt, are lost from the body, it is possible, by drinking a large amount of fluid, for the patient to suffer from water intoxication, and from dehydration at the same

time. However, if water retention and salt retention co-exist, it is impossible to produce intoxication. Clinically, this condition is characterized by headache, nausea, asthenia, muscular irritability, salivation, convulsions and ultimately death. There has only been one fatal case reported in the literature, however, and here the condition was only recognized at autopsy. In the case in question, following a cholecystectomy, a patient had received 9 Litres of tap water by proctoclysis. The above symptoms soon developed and the patient died. At autopsy, there was little abnormality beyond a great increase in the weight and size of the brain. The immediate cause of death was "oedema of the brain."

The importance of salt in the content and distribution of body water has already been pointed out, as was the fact that osmotic equilibrium between intracellular and interstitial fluid was attained, not by a shift of electrolytes, but by a shift of water. If then the concentration of electrolyte in the extracellular fluid decreases, water passes into the cells by osmosis, and the cells swell. If large amounts of water are given rapidly to a person with a normal salt concentration, in the extracellular spaces, this concentration decreases due to dilution, water passes into the cells, and mild symptoms of water intoxication result. If the individual has already suffered a depletion of electrolytes, the symptoms are produced by a correspondingly smaller amount of water.

Eventually convulsions occur due to the increased water content of the brain cells. Treatment, of course, is by the rapid administration of salt, usually as a hypertonic intravenous solution.

2. The problem of *edema* has been left severly alone as it is beyond the field of this subject. However, there is one aspect that should be mentioned. Coller and Maddock have shown that the *routine* administration of saline to surgical patients often results in a measurable amount of edema. The only reason that the edema is not more severe is the fact that most "routines" only last for 2 or 3 days. The intravenous administration of fluids represented a tremendous advance in medical sciences, but like all such advances, too free use has been made of it, and abuse is frequent. The routine administration of fluid to a dehydrated patient is the biggest example of such abuse. Each patient presents a different problem and must be treated as such. If salt has been lost, salt must be administered -- not a toxic dose of water. If water has been lost, the patient must be given water, not a solution of salt, that may overburden an already weakened heart.

3. Passing to the other extreme, we have the condition of *dehydration.* There is no surgical condition more dangerous to the patient, and all other procedures must be held in abeyance until this factor is corrected.

Applying the physiological principles already outlined, dehydration can be seen to be a result of:

(1) Decreased fluid intake.
(2) Increased fluid output.
(3) A reduction in the total quantity of body electrolyte.

The effect of a decreased fluid intake is obvious, as is the case with an increased output. However, unless the fluid exchange of a patient is accurately recorded, important variations in intake or output are apt to be overlooked. Coller and Maddock have shown that the output in particular is very apt to be underestimated. These workers demonstrated that in many operations, due to the high temperature of the operating room and the covering blankets and drapes, as much as 2 or 3 litres of fluid may be sweated away. Add to this the fluid loss due to faulty hemostasis, and another litre, sweated away in the immediate postoperative period when the patient is bundled up in blankets and surrounded by hot water bottles, and dehydration is well on the way without the surgeon realizing it. Despite the importance of intake and output *the* factor that produces dehydration,

is the total quantity of electrolyte in solution, since this is what controls the total amount of body water. There is a very important physiological requirement for a nearly stationary concentration of salt. Any loss of electrolyte is followed by excretion of water, till the normal concentration is again reached. From this it follows that a decrease in the volume of body water is an indication of a deficit in the level of body electrolyte; and that any loss of body water must be explained in terms of loss of substance from the body. From this point of view dehydration is seen to be a somewhat inadequate term since it fails to indicate the primary event, which is removal of electrolyte.

The ultimate cause of dehydration then is most often a decrease in the body salt, and any factor causing this will cause dehydration. Electrolyte may be lost in large quantities in diarrhea, vomiting, fistulae, polyuria, hemorrhage, inordinate sweating and other conditions. Less apparent is the dehydrating effect of pure water. If 1 Litre of water is ingested, in two or three hours 1 litre of urine is excreted. But urine is a saline solution and the effect of the water has been to wash out a certain amount of body salt. As a result more water is excreted and a certain amount of dehydration has occurred. The result is no better if concentrated saline is taken. Here excess salt must be removed and as it cannot be excreted in a concentration greater than 2%, water is again lost to the body.

Clinically, symptoms of dehydration appear when 6% of the body weight has been lost. These symptoms include intense thirst, decreased salivation, dry tongue, sunken eyes, oliguria, and dry inelastic skin. As the body water is reduced, loss of weight occurs and the acid base balance is disturbed. The interstitial fluid provides a protracted defence of the intracellular and the vascular compartments, but ultimately this reservoir is depleted. At first water is lost in order to maintain the concentration of electrolyte but eventually the need of the body for fluid becomes so great, that the non-electrolyte urea is retained instead in order to maintain the osmotic pressure. The result is an increase in the blood. N. P.N.

When the electrolyte lost to the body is chloride ion, as has already been pointed out, compensation occurs due to an increase in bicarbonate ion. Provided there is plenty of water available, there is no dehydration as there has been no decrease in the concentration of electrolyte. However, when sodium is lost, either with or without chloride, there is no electrolyte to replace it, and there is a decrease in the concentration of body electrolyte. The result is dehydration, and eventually an increased blood urea. Free administration of water in such a case can have no effect on lowering the N.P.N. or decreasing the dehydration.

C. — Conclusion

It is manifestly impossible to adequately cover this aspect of water balance in such a short space, and any attempt to do so inevitably causes confusion. In a rather belated attempt to crystallize the clinical applications that have been discussed, I should like to consider briefly the treatment of a dehydrated patient requiring parenteral fluid.

1.—Since there is dehydration, at least 6% of the body weight has been lost. This must be restored by the administration of the appropriate amount of normal saline 3600 c.c's in a 60 Kg man.

2.—The patient now having a normal water content, every effort must be made to maintain that state. This is done by administering an amount of water (as 5% glucose) equal to the daily loss.

(a) The loss through the skin amounts to 2000 c.c's per 24 hrs.

(b) The loss through the kidneys should amount to 1500 c.c's per 24 hours. If it doesn't then expect dehydration.

The total loss in this manner amounts to 3500 c.c's of water, and so we must replace it with 3500 c.c's of 5% glucose. To this daily requirement must be added any water or salt, that is lost from abnormal sources such as in faeces, vomitus, or blood. By this means the patient can be kept in proper water balance indefinitely without the development of edema, intoxication or dehydration: provided his serum protein is at a normal level. But that is another story.

An extensive bibliography may be seen upon request.

WATER BALANCE AND ITS RELATION TO SURGERY

PART II.

By L. J. LESTER, B.A., '39

Water balance is a subject which in recent years has been recognized as of great importance to the welfare of the patient, especially in surgical conditions. Upsets in water balance and the means of correcting those upsets are therefore worthy of some study. To the casual student there seems to be little need for such a study. It is accepted that dehydration is a serious condition which should be combated, and intravenous glucose in saline is routinely ordered. However, surgical conditions can not be treated with optimum results by the use of such a routine. Dehydration accompanies many different clinical entities, and to treat it properly one must understand the pathological and chemical changes which have taken place. Therefore, some of these changes will first be considered. Fluid loss occurs in three main groups of conditions.

A. Loss of Fluid Directly From Blood Stream

1. *Haemorrhage.* We are considering only sudden massive haemorrhage. The body loses whole blood, so that there is a decrease in circulating volume. This is compensated by a peripheral vaso-constriction to fit the vascular bed to the reduced volume. At the same time there is a diffusion of extra-cellular tissue fluid into the vascular system in an attempt to keep the blood volume constant. There is therefore a dilution of the R. B. C. which remain, and this dilution is the most characteristic feature of haemorrhage.

2. *Shock.* Shock may resemble haemorrhage clinically, and often the picture is confused by the presence of both together. Actually, it can be shown that the two are quite different. Two varieties of shock are recognized. (a) Primary Shock — occurs immediately after trauma and is due to a reflex dilation of the peripheral vascular system. The circulating blood is poured into dilated capillaries, so that the effective blood volume is greatly reduced. (b) Secondary Shock — is the type usually encountered. Here too there is a capillary paralysis, but it is of peripheral origin and does not depend on any nervous mechanism. In addition, plasma leaks out through the capillary endothelium into surrounding tissue spaces. The resulting low blood pressure and stasis anoxia, cause a further increase in capillary permeability, so that a vicious circle is established. Fluid, electrolyte and protein diffuse out. There is therefore a concentration of red cells with a high red count and Hb. This haemoconcentration is the main distinguishing feature from haemorrhage.

B. Loss of Fluid by Way of G. I. Tract

This may occur in all forms of intestinal obstruction in which vomiting is present, in diarrhoea, or in fistula of

the gastro-intestinal tract. Further, it may occur in lower intestinal obstructions *without* vomiting. Fluid which collects in the stomach or intestines is really lost to the body whether it is vomited or not. Hence one can draw little comfort from the fact that a patient with a suspected obstruction is not vomiting. The total amount of secretion which is poured into the lumen of the gut is 7-10 litres per day. Practically all of this is normally reabsorbed. If reabsorption does not occur, the loss of fluid to the tissues may be tremendous.

Gamble has shown that the intestinal secretions have approximately the same electrolyte concentration as the blood serum. They only differ from each other in the various proportions of individual ions they contain. In considering obstructions at various levels, one finds that the upset in electrolyte balance depends on which secretions or combination of secretions is lost. In all of them there is a loss of fluid, and dehydration. In pyloric occlusion, mainly HCl from the stomach is lost, i.e., chloride ion, and very little sodium. The excessive loss of acid radicle causes an increase in alkali reserve, or alkalosis. In the duodenum the alkaline pancreatic secretion and bile are added. Therefore an obstruction below the ampulla of Vater gives a loss of considerable Na as well as Cl. The result would be tendency to acidosis, although there is usually enough Cl loss from the stomach to cause an alkalosis with all upper jejunal obstructions. As we descend in the intestine, more and more alkaline secretion is produced and more and more Na is lost when obstruction occurs. Hence in lower small bowel obstruction there is usually more tendency to acidosis. Obstruction in the large bowel, and also diarrhoea, give a predominant loss of alkaline secretion which results in an acidosis. The type of acid base upset with intestinal fistulas depends similarly on their location. A duodenal fistula with marked loss of alkaline pancreatic juice will cause an acidosis. The loss of bile is usually well borne since it is only mildly alkaline. An exception to this rule is seen in biliary obstruction due to CA of the head of the pancreas. In this condition, if the bile is drained the patient will probably die in a few days. The reason for this was not suspected until studies were made on the bile lost through drainage. Walters of the Mayo Clinic found that in draining a common duct with a stone in the ampulla, 500-700 c.c. of bile were lost in 24 hours. However, when CA of the head of the pancreas was the cause of the obstruction, drainage resulted in a loss of 1300 to 1800 c.c. per day. Furthermore, the bile drainage from the duct in CA of the head of the pancreas contains several times as much sodium chloride as compared with that lost when stone is the cause of the obstruction. The body therefore loses a considerable amount of salt and water, and unless one appreciates the seriousness of this loss, the patient whose biliary tract is drained in the presence of obstruction due to CA of head of pancreas, will go rapidly downhill and die.

The accompanying blood changes in the above conditions are of importance. In dehydration, there is a haemoconcentration with increased RBC and Hb. In alkalosis from high obstruction, there is a low plasma chloride. In acidosis from low obstruction there is a low CO_2 combining power. With an intermediate obstruction and no upset in acid-base balance, the blood chloride level may be normal. However, one can only determine the concentration of chloride per 100 c.c. plasma and even though this be normal there may still be a great depletion of the total chloride of the body.

C. Miscellaneous Fluid Loss.

1. Massive Burns. Besides the initial shock water is lost very rapidly by evaporation from weeping ulcers.

2. Long continued Massive Purulent Drainage gives a loss of fluid, electrolytes and protein.

3. Diabetes Mellitus is characterized by a tendency to dehydration. The

latter is due to two factors. (a) glycosuria, (b) the base which is required to neutralize the ketone acids carries with it some body water when it is excreted by the kidneys. Hence diabetes should receive pre-operative glucose and insulin to combat ketosis, as well as fluid for prevention of dehydration.

Principles Involved in Replacement Therapy.

Water by itself will not correct dehydration. In fact it acts as a dehydration agent by washing out some salt in the urine, and along with this some body water which can no longer be retained when its salt content is removed. Administered water can only be retained if an equivalent amount of salt is given at the same time, so that the electrolyte concentration in the body will remain constant. In giving isotonic saline, if more water is needed and less salt, then the excess salt is excreted in the kidneys. For this purpose extra water should be supplied as 5% glucose. 5% glucose is itself isotonic, but cannot be used in place of salt solution to correct dehydration. The glucose is burned and water left behind, which only further aggravates the dehydration because it cannot be retained. To correct the acidosis or alkalosis, one should add the proper neutralizing salt. Actually this is not necessary, because if NaCl is given in sufficient quantity, the kidney retains whichever ion the body needs and excretes the other. This selective excretion is only possible if there is enough water for adequate urinary volume.

With these few basic principles as a start, we can tackle the practical problem of correcting dehydration in various clinical conditions. In haemorrhage, there is loss of blood volume and the ideal replacement is blood transfusion. In shock although there is no actual loss to the outside, yet the circulating volume is markedly decreased. Further, there is a tendency for fluid to leak out from the paralyzed capillaries as quickly as it is given intravenously. To remedy this the therapeutic fluid should contain a colloid which exerts a retentive osmotic pressure. The best available colloid is blood and therefore transfusion is the best treatment. Its disadvantage is that it increases the haemo concentration and thus throws an increased load on the heart. In milder cases it is often sufficient to give intravenous fluid other than blood in an attempt to raise the circulating volume.

The two most important surgical problems relating to fluid balance are (1) water maintenance when fluids cannot be taken by mouth, especially post-operatively, and (2) the rehydration of a patient admitted to hospital in a state of dehydration. To elucidate the first problem, Coller and Maddock studied the water loss of the ordinary surgical patient during and after operation. Several interesting facts were ascertained. The blood loss alone was found to vary from 10 c.c. to 1,200 c.c. and was usually much greater than what the surgeon thought. In addition to blood, considerable water was lost in the post-operative period from insensible perspiration and sweating. On the average they found the total fluid loss during operation and four hours post operatively to be about 1,000 c.c. In other words, one may say that the surgical operation itself costs the patient one litre of fluid.

The loss of water through insensible perspiration was then determined during convalescence by keeping an accurate check on input and output, and weighing the patient daily. Fluid intake includes not only fluid, but water present in solids plus water of oxidation of foodstuffs, which may amount to 2-300 c.c. per day. By such experiments the insensible perspiration was found to reach the impressive total of 2,000 c.c. per day. This figure is exclusive of visible perspiration. Furthermore, in hyperthyroid patients, or in the presence of fever, this amount

may be considerably larger. However, one can accept 2,000 c.c. as the average for most surgical patients.

Finally, one must allow for water loss in the urine. With healthy kidneys working at maximum efficiency 600 c.c. urine per day may be enough to rid the body of waste products. However, to be on the safe side and allow for possible decreased kidney function, one should allow 1,500 c.c. of urine for adequate excretion. Adding this to our insensible loss of 2,000 c.c., gives us a total of 3,500 c.c. per day. Coller and Maddock have accepted this figure, 3,500 c.c., as the minimum amount of fluid which a surgical patient needs daily to replenish his loss. This is only a basal loss and to it we must add the volume of fluid lost by other sources, e.g., vomitus, aspiration, drainage, perspiration, etc. It is thus seen that the total fluid needs of a patient may be quite considerable, even up to 5-6 litres per day.

Having determined the total fluid volume, in what form should it be administered. It is necessary to use an isotonic solution since distilled water will cause haemolysis of red cells. 5% glucose is isotonic and the glucose is also essential in preventing starvation ketosis and supplying calories. Therefore such a solution can be given with advantage. The question of the need of salt in the fluid is not so simply settled. All too frequently normal saline is the routine vehicle for fluid administation. A little reflection shows how unphysiological this is. The normal salt intake of an individual is 6-8 grams per day. If the intake is reduced to zero in a healthy person, the salt excretion in the urine quickly drops to a low figure, so as to conserve the supply, and the individual can carry on for weeks with no ill effects. In other words, a surgical patient who is not losing salt by abnormal channels can get along quite well with no salt intake for a few days, and if he received his usual 6-8 grams per day this supply would certainly be adequate. Yet in spite of this many patients receive 3-4 litres of normal saline per day, containing 25-35 grams of salt—which is very much more than they need. In old individuals with impaired kidneys, this may be very dangerous. The incidence of post-operative oedema from injudicious administration of normal saline is much more real than apparent. Jones and Eaton have shown that oedema of this type occurs first in the internal viscera, and by the time it becomes clinically manifest, the patient is actually waterlogged. Furthermore, the low serum protein which tends to be present because of undernourishment further aggravates the tendency to oedema. This incidence of oedema in the viscera is certainly not of mere academic interest. The nutrition of tissues is undoubtedly impaired. Mecray has also shown that the emptying time and motility of the stomach is greatly retarded. Furthermore it has been shown that obstruction may occur from oedmatous swelling of the gut, and such oedema not uncommonly is the cause of malfunction of a gastro-enterostomy. Hence there is every reason for being cautions in the administration of saline. Not more than one litre of the required 3,500 c.c. should bs in the form of .85% sodium chloride with 5% dextrose. For the remainder, 5% dextrose is sufficient. In a survey of surgical patients at University Hospital, Ann Arbour, Coller found that 80% were receiving intravenous fluid because of their inability to take it orally, and only 20% were receiving it as replacement for fluid lost to the body by abnormal means. Fluid lost by vomiting or drainage has approximately the same Na Cl content as blood, and therefore this should be replaced by normal saline. But in 80% of patients 5% dextrose would be adequate for their needs.

To recapitulate the post-operative treatment: The average patient needs 3,500 c.c. fluid per day of which one litre as glucose in saline is sufficient, the remainder being given as 5% glucose only. In addition he should have

all abnormal fluid loss replaced volume for volume by normal saline. If post-operative oedema does develop, salt administration should be stopped and 5% glucose continued alone. There is no need to stop water administration since as has been pointed out before, it alone cannot produce oedema and in fact acts as a dehydrating agent.

The second major problem which is to be considered is the correction of dehydration as one sees it in patients admitted, for example, with intestinal obstruction and persistent vomiting. In correcting the water balance of a person who is dehydrated, one must supply him with a volume of water and salt equivalent to that which he lost. When the loss is known, e.g., a measured amount of vomitus, then we can replace it volume for volume with normal saline. Usually, when a patient is admitted, his quantitative loss is not known and there is no way of measuring his dehydration. It has been shown that when a patient exhibits clinical signs of dehydration, he has lost at least 6% of his body weight as fluids. One can therefore rehydrate an individual by giving him 6% of his body weight as normal saline, plus his usual daily requirement. However, this is an inaccurate means of estimation since 6% is only a minimum value and one may need 8 or 10% of body weight as fluid. Recently, Coller and associates have evolved a more accurate means of dehydration. It is only applicable to high intestinal obstruction where the hypochloraemia is a feature. It is based on the following principles. The plasma chloride level is directly proportional to the tissue chloride level. Hence a certain drop in plasma chloride indicates a relatively similar drop in the total chloride of the body. Sherman has calculated that the total body chloride is ¼ of 1% of body weight, i.e., 175 grams for a 70 kilo man. Normal plasma chloride is 560 milligrams %. If this value drops to 450, i.e., a decrease of 20% from normal, there must be a similar 20% decrease of total body chloride. Therefore 20% of 175 grams, or 35 grams of salt, have been lost. To replace 35 grams of salt in the form of normal saline (which contains 8½ grams per litre) one would need 4 litres of normal saline. One can thus calculate from the drop in plasma chloride how much saline is necessary to rehydrate a person. Coller has applied this principle to surgical patients and found that the calculated amount of saline was just sufficient to correct dehydration and bring the plasma chloride up to normal.

To simplify the formula, he suggests that one merely give .5 gms. salt (as normal saline) per kilo body weight, per 100 mgm. % drop in plasma chloride. This would amount to a little more saline than the amount calculated above, but this is advantageous as it allows for the plasma chloride levels appearing higher than they really are because of haemoconcentration. There are several difficulties in the use of such a mathematical rule for water replacement. In calculating the patient's weight one should add 6 to 10% to allow for dehydration. Furthermore, if sodium is lost in equal or greater amount than chloride (as occurs in low obstructions) then the plasma chloride levels are normal, even though the body chlorides may be greatly depleted. In such a case one must revert to giving 6% or more of body weight to achieve rehydration and can then maintain it by replacing it by the abnormal loss volume for volume with normal saline.

It is common practice to administer hypertonic saline to cases of high intestinal obstruction with low plasma chloride when they are admitted in a state of dehydration. The rational of this therapy is that hypochloraemia itself gives rise to symptoms which may partly or wholly explain the patient's malaise, and hypertonic saline serves to correct this rapidly. However, from the point of view of water balance, this procedure is open to question. Hypertonic saline, especially when given rapidly, dehydrates the

tissues. Furthermore it stimulates marked peristaltic action of the gut which may result in diarrhoea and further loss of fluid. Hence, if hypertonic saline is used at all, it should not be too concentrated, say 2½%, and should not be given very rapidly.

In conclusion one would like to emphasize the importance of understanding the exact nature of disturbance in water balance. Surgery is now far more than a mere technical procedure and it is our hope that this paper has illustrated the importance of a knowledge of the biochemical upset in the management of surgical patients.

The author wishes to acknowledge the helpful criticism of Dr. J. H. Couch in the preparation of this paper. An extensive bibliography may be obtained on request.

THE RETICULO-ENDOTHELIAL SYSTEM IN RELATION TO HODGKIN'S DISEASE

By R. A. G. LANE, '39

Prior to Aschoff's time, the component cells and fibres of the reticulo-endothelial system had been described but it was Aschoff himself, who collected the nondescript group into a definite system. The real significance of this tissue was not realized until the experimental use of vital dyes. At first accidentally and then experimentally it was discovered that these cells had the power to act as scavengers, picking up and storing electronegative particulate matter. The latter included cell debris from catabolism, various forms of bacteria, carbon particles and degenerate red blood cells, including the experimental dyes. Following this lead the anatomical distribution of the reticulo-endothelial cells in the body was fairly carefully defined. Finally painstaking investigation revealed the genetic relationships of the various cells. The story of this system is by no means complete. The physiology and the role played in disease are becoming more apparent. As soon as more is definitely known about certain details of the system, a standard nomenclature will be a great value. As one author points out, "The same cells are called different names by different people and different cells are called by the same names. Added to this is the factor that there is honest disagreement about the origin of certain of these cells, their developmental potentiality and the genetic relationship between them. The confusion caused by this combination of man-made and natural difficulties almost guarantees utter frustation to the casual student."

The term 'reticulo-endothelial system' is a misnomer because true endothelial cells play no essential role. Endothelial cells, according to Maximow, are individual cells with definite boundaries and their potentiality is limited to self-reproduction and the formation of fibroblasts. Reticular cells have a direct origin from the mesoderm, possess multipotential capacities and are the cells of significance, both in the reticulo-endothelial system and in Hodgkin's disease. At this point, a definite understanding must be made apparent. The primitive reticular cell is the stem cell of haemopoeitic tissue, and it is responsible for development of the two cells — the haemocytoblast, which goes on to form blood cells and the ordinary reticular cell, which goes on to form the cells of the reticulo-endothelial system. The close relationship of the reticulo-endothelial system to the haemopoeitic system is then

realized. It is probably best not to include the primitive reticular cell in the reticulo-endothelial system for the following reasons — the primitive cell is not a phagocytic cell, it has more potentiality whereas the ordinary cell is more specialized and phagocytic. It has not been made clear in the literature that the undifferentiated mesenchymal cell is in all probability analgous to the primitive reticular cell.

Anatomical Distribution

The anatomical distribution of the system will be considered in four groups, paying less attention to the first three, which are better known.

(a) *Reticulo-endothelial cells* of the spleen, bone-marrow, lymph nodes, liver, pituitary and adrenal cortex. There are the fixed, lining-cells of the sinusoids in all these organs. Also there are the free cells, which are loosely held in the reticular meshwork of the first four of the listed organs. The fixed forms have the ability to become transformed quickly into amoeboid forms, and vice versa.

(b) *Macrophages of the tissues,* or the histiocytes of Maximow. These cells, which are quite as active as those of the preceding group, are also present in sessile and wandering forms.

(c) *Monocytes of the blood.* There is more question as to whether these cells are to be included. However, most authors believe they should be. As soon as they leave the blood stream, they are seen to become actively phagocytic.

(d) *Reticulo-endothelium of other organs.*

(i) *Lungs*: Alveolar phagocytes (dust cells, heart failure cells) are believed to be reticular in origin. They are best seen at work when handling carbon or silica particles, and in the disposal of alveolar extravasated blood in heart failure. In resolution of pneumonia, the exudate has, as its predominant cell, the monocyte rather than the polymorph as previously.

(ii) *Heart*: In the interstitial tissue of the normal myocardium, can be distinguished cells, which bear a close resemblance to reticulo-endothelial cells. They concern themselves with the normal defence reactions of the myocardium and are the essential elements of the Aschoff nodule of rheumatic myocarditis.

(iii) *Female genital tract*: In the wall of the uterus and in the parametrium are certain reticular cells, which are concerned with local defence reactions during pregnancy and puerperium and for the resorption of postpartum products. During the development of pregnancy, in addition to the hypertrophy of the myometrium, there is a recognized new formation of muscle fibres. In the first few months, new muscle fibres develop from pre-existing macrophages, later from adventitial cells (macrophages collected around the adventitial coats of blood vessels) and from newly-developed macrophages and finally also from fibrocytes. After delivery the newly-formed muscle fibres disintegrate and the macrophages then act as scavengers.

(iv) In addition to those cells already mentioned under this group, the *microglia* are to be regarded as the counterpart in the central nervous system. Reticulo-endothelial cells are also present in glands of internal secretion, and in the serous cavities. Just how general the distribution of reticulo-endothelium is, may only be surmised, but evidence points to the fact that it is more extensive than at present suspected.

Histogenesis

The stem cell of haemopoeitic tissue and of reticulo-endothelial tissue, is the primitive reticular cell of alternately, the undifferentiated mesenchymal cell. The great potentiality of these cells may be realized by the following description.

(a) Bone marrow. The primitive reticular cell specializes by turning into the ordinary reticular cell, which then has phagocytic powers, the ability to make fibres and ability to become wandering elements, the free macro-

phages. They also may be adapted to form sinus-lining cells, aptly termed by Maximow, littoral cells. The second mode of differentiation is to form the haemocytoblast, which in turn goes to form the granular leukocytes, the erythrocytes, and the megakaryocytes.

(b) Lymphoblastic tissue. The primitive reticular may form various reticulo-endothelial elements, just as described under bone-marrow. Also, it produces cells of the lymphocyte series. From the latter the monocytes probably have their origin.

In its resting state the reticulo-endothelial system gives no clue as to its potentialities. It possesses multipotential capacities, which are retained in adult life, just as the mesoderm from which it arises. To obtain a picture of the dynamic potentiality of this tissue, the pathological lesion of Hodgkin's disease may well be used. Here we see the many-sided phases in the life history of a lympho-reticulo-endothelial group of cell, from the primitive cell progenitors up to the terminal fibroblastic changes.

The Hodgkin's Lesion

The Hodgkin's lesion is a proliferative one affecting reticulum, and all the cellular manifestations, which are recognized as characteristic, may well be due to the subsequent differentiation of the one type of cell, the primitive reticular cell. Since Sternberg's description the proliferation of the reticular cell, together with the multinucleated forms it assumes, has been recognized as the essential microscopic feature of the disease. Various workers have been able to trace all cells and fibres of the lesion to the primitive stem cell.

The pathological picture may be conveniently separated into four phases, according to the time development. Phase one is concerned with a proliferation of the reticulo-endothelial and lymphocytic tissue, with some stimulus giving proportional overgrowth of the cell types. Phase two consists of a disturbance of the natural evolution of the lympho-reticulo-endothelial group so that numbers of immature forms appear. Phase three consists of the development of the protective cell elements, the eosinophiles, the multinuclear cells and the large mononuclears. Phase four is a conversion of the cell elements into fibrous tissue. The essentials of the pathological picture are the replacement of the normal architecture of the lymph node or other tissue, by one or more of the following — (a) Hyperplasia of the reticular cells. (b) Presence of multinuclear cells. (c) Excessive fibrosis. Certain features, not essential, are charactertistic and are the eosinophiles, the reticular cells or fibres and the multinucleated giant cells.

Discussion

In a consideration of the cause of any disease, it would be wise to remember the advice of William Harvery in "De Generatione" — "There is but one road to science, to wit, that we proceed from things well known to things less well known, from things manifest to things, more obscure." Have we an explanation of the cause of Hodgkin's disease, based on a study of the genetic relationships of the component cells and fibres of the lesion? Let us assume that the primitive reticular cell is subjected to some abnormal influence causing progressive proliferation. Once that proliferation has been established and maintained, the subsequent cell pathology can be accounted for by the differentiated cells of the one stem cell. The term 'abnormal influence' may carry only a miasmatic meaning but remember this saying, "So long as the exact nature of what constitutes neoplasia and the influences which initiate the change are unknown, so long must the criticism of those, who adhere to the neoplastic theory regarding the origin of Hodgkin's disease, be guarded." This abnormal influence may be re-

lated to the effects of the large virus of Gordon, or to some other factor, not yet apparent. Similar effects have been noted in the Rous sarcoma and in other experimental tumours.

An analogy may be drawn to two other lesions, that of osteogenic sarcoma and of leukaemia. For years confusion has reigned in the field of certain bone tumours because of the failure to recognize a genetic classification of such. The stem cell of osteogenic sarcoma is the undifferentiated mesenchymal cell, which, as it specializes, produces the various cell elements seen in that sarcoma. In the leukaemias, the disturbance is higher up in the genetic relations for they are proliferations of a partially-differentiated cell. In this respect, the disturbance in Hodgkin's disease lies somewhere between that level and the level of the totipotential tumour.

Summary

The reticulo-endothelial system has been briefly described, chiefly to elucidate certain points of pathogenic interest in Hodgkin's disease. A theory of cause for the latter has been suggested, with the intimation that, if the lesion can be explained on an anatomical and genetic basis, resort should not be made to further-removed possible causes. Just as in general cancer research, much attention is being focussed on the "abnormal influence" underlying the disease process itself. The most recent experimental work in connection with Hodgkin's disease has been concerned with the role of the eosinophile in the Gordon test and in the carriage of histamine.

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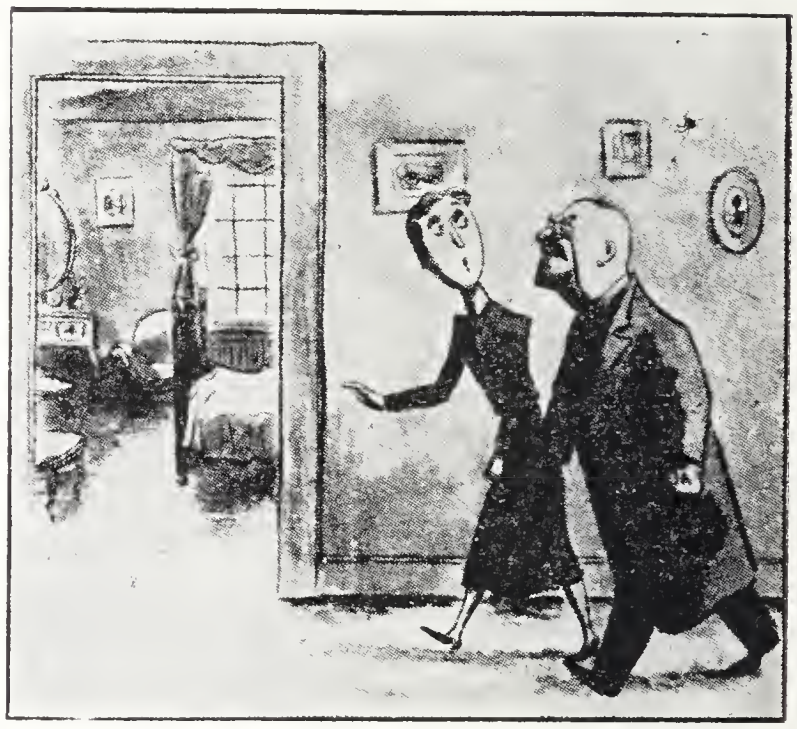

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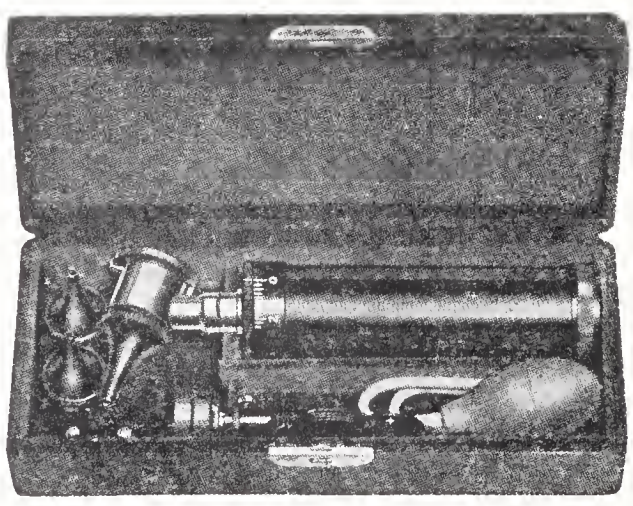

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TESTS OF LIVER FUNCTION

By T. A. FRASER, B.A., '40

The liver is the seat of a diversity of physiological functions. It is also subject to many pathological processes and the attempt will be made to differentiate these on the basis of alteration of function as shown by liver function tests. Some of these tests have been of value in the elucidation of the nature of the diseases; some are of use clinically.

The main problem in the diagnosis of liver disease is the differentiation between jaundice requiring surgical from that requiring medical treatment; painless jaundice may be due to obstruction of the bile duct, by a silent stone or by compression from carcinoma in the head of the pancreas, or it may be due to catarrhal jaundice. The history and physical examination, which are usually adequate for the diagnosis of liver diseases, may require supplement in this differential diagnosis and many liver function tests have been proposed to fill this need.

The usefulness of these tests is limited in several ways; in catarrhal jaundice, where both damage of the liver parenchyma and obstruction of the biliary tract occur, the findings are not decisive; the functional state of the organ cannot be determined from a single test as this involves only one of a wide variety of functions which may not be disturbed equally; finally, the liver has a great functional reserve and the tests now available are not sensitive to minimal liver damage.

Bile Pigment Metabolism

The first function of the liver to be considered is in relation to bile pigment metabolism because derangement gives the striking physical sign of jaundice and because the tests of this function are readily performed.

Bilirubin is elaborated mainly, if not exclusively, from blood haemoglobin. It is formed in the cells of the reticuloendothelial system; excreted from the blood stream by the parenchymal liver cells; collected into the biliary tract and passed into the duodenum. In the gut, through the action of bacteria, it is reduced to urobilinogen. Part of this urobilinogen is lost in the stool, part is absorbed into the portal system; of this, almost all is excreted by the liver parenchyma in the bile and the remainder is excreted by the kidneys and is lost in the urine. Evidence of disturbance of this process is looked for in the blood, urine and feces.

Bilirubinemia: The level of bilirubin in the blood may be found high because of destruction of red cells in excess of the excretory capacity of the normal liver, because of damage of the parenchymal cells with defective excretion or because of obstruction in the biliary tract with resorbtion of the bilirubin into the blood stream. The level of bilirubin cannot accurately be estimated from the degree of jaundice; it may be elevated before the appearance of jaundice and have returned to normal while the epithelial tissues are still yellow. Direct examination of the blood bilirubin is of further value in that it gives some indication of the primary cause of the jaundice.

The *van den Bergh reaction* depends on the formation of a reddish violet colour when the diazo reagent is added to serum containing bilirubin. In the prompt direct reaction the colour develops at once, which is commonly taken to indicate that the bilirubin has passed through the parenchymal cells of the liver. In the delayed direct reaction, which indicates that the bilirubin has not passed through the parenchymal cells, the colour develops only after a latent period, if at all. If both types of bilirubin are present,

colour appears at once but the maximum intensity is reached later; this biphasic reaction is not significant clinically. In practice the test is useful in differentiating, not between the jaundice of obstruction and of parenchymal damage, but between the jaundice of excess haemolysis where the reaction is delayed direct and of liver or biliary tract disease in both of which the reaction is prompt direct.

The indirect reaction measures the concentration of bilirubin independently of type. The diazo reagent, alcohol and saturated ammonium sulphate are added to the serum; the proteins thus precipitated are separated by centrifuging; the bilirubin dissolves in the alcohol and reacts with the diazo reagent. The concentration of bilirubin is measured by the intensity of colour developed which is determined by colorimetric comparison with an artifical standard. The normal level is between .2 and .5 units; it is usually stated that jaundice becomes clinically evident when it rises above 4 units, although this varies with the complexion of the patient.

In some clinics a determination of the *icterus index* is the routine procedure. In this test the intensity of the yellow colour of the serum is compared directly with a standard solution of potassium dichromate. The normal range is below 10 units. Even slight hemolysis interferes with the estimation and the occasional presence in the blood of carotene, a pigment found in orange juice and many vegetables, gives misleading readings.

Bilirubinuria: When bilirubin appears in the urine the patient is clinically jaundiced. Bilirubin which gives the prompt direct van den Bergh reaction is detected in the urine when the bilirubinemia reaches some 4 units; that giving the delayed direct reaction, only when the bilirubinemia is around 12 units, which is rarely reached in hemolytic jaundice. If the patient is jaundiced and the test shows no bilirubin in the urine, the hyperbilirubinemia is almost certainly of haemolytic origin.

The presence of bilirubin in the urine may be suspected from inspection. The usual chemical tests depend on the production of coloured oxidation compounds with nitric acid. A more sensitive test is to add barium chloride solution to the urine which must be slightly acid, and filter; to the material retained on the filter paper is added Fouchet's reagent which contains trichloracetic acid and ferric chloride; a green or blue colour develops if bilirubin is present.

Urobilinogenuria: The urobilinogen in the blood is derived almost entirely from the gut where it is formed from bilirubin. It is removed from the blood by the liver and kidneys. In the presence of parenchymal damage, the excretion by the liver is diminished and the level in the urine, where it is normally found only in traces, rises. It may also be increased from overproduction in haemolytic jaundice; abnormally large amounts of bilirubin reach the gut and urobilinogen is formed and absorbed in excess of the excretory capacity of the liver. Rarely it is increased in obstructive jaundice.

The usual tests for urobilinogen are not positive unless it appears in abnormal amounts. It is detected by oxidation with iodine to urobilin which produces fluorescence in the presence of zinc salts.

Examination of the stool: When the bile passages are completely obstructed, which may be due to intrahepatic blocking as in catarrhal jaundice as well as extrahepatic, no bile reaches the gut. The feces consequently contain none of the reduction compounds of bilirubin; this is evident in the clay colour or may be shown by chemical tests.

Dye Excretion

Various dyes, in a manner similar to bilirubin, are taken up by the reticuloendothelial system and excreted specifically by the liver in the bile. When the parenchyma is damaged, an

injected dye is excreted at a slower rate. These tests may be used only in the absence of jaundice.

The *bromsulfalein test* is performed by intravenous injection of 5 milligrams of the dye per kilogram body weight; blood samples are removed from the opposite arm at the end of 1 and 30 minutes. The concentration of the dye in the samples is determined by treating the serum with sodium hydroxide and making colorimetric comparisons. Retention of more than 10 per cent. of the dye at 30 minutes is considered abnormal.

The *rose bengal test* involves the intravenous injection of 10 c.c. of a 1 to 2 per cent solution of tetraiodotetrabromfluorescene; samples are taken at the end of 2 and 8 minutes and colorimetric determinations made. The presence of 50 per cent or more of the dye in the 8 minute sample is taken as evidence of parenchymal damage.

The *bilirubin excretion test* is more appealing in that it measures the response of the organ to strain on a physiological process. Bilirubin to the extent of 1 milligram per kilogram body weight is injected intravenously and samples taken at 5 minutes and 4 hours. Retention of 6 per cent at the end of 4 hours is the upper limit of normal.

Carbohydrate Metabolism

Monosaccharides absorbed from the gut are carried in the portal blood to the liver where they are converted into glycogen. Parenchymal disease leads to decrease of this conversion and the sugar accumulates in the blood stream. Sugars such as glucose and levulose are utilized readily by the liver and also to some extent by muscle tissue. Galactose is more suitable for a test in that it is taken up exclusively by the liver, and here only with difficulty, so the effect of deranged liver function is greater; the kidney threshold for this sugar is low and the sugar not utilized appears in the urine; the metabolism of galactose is influenced much less by insulin than is that of glucose or levulose.

The *galactose tolerance test* has gained the most general acceptance of all the tests of liver carbohydrate metabolism. After a 12 hour fast the subject is given by mouth 40 grams of galactose in 250 to 500 c.c. water. The urine formed in the next five hours is collected and the galactose content estimated. Normally the amount excreted rarely exceeds 2 grams; the excretion of any amount greater than 3 grams in the five hours is considered evidence of damage to the liver parenchyma.

The *levulose tolerance test* is performed similarly on the fasting subject by administration by mouth some 40 grams of the sugar in 250 c.c. water. The fasting blood sugar is determined and the blood sugar at 30 minute intervals for 2 hours. Disease of the liver parenchyma is evidenced by a rise of blood sugar of 30 to 40 milligrams per cent, or elevated blood sugar at the end of two hours. The details of administration and criteria of abnormality vary among clinics.

Another test depends on the removal of intravenously injected sodium *d*-lactate from the blood stream by the liver where it is converted into glycogen. Other tests follow the blood sugar after giving glucose, glucose and insulin, and so on. Each test has a vigorous proponent.

Fat Metabolism

The liver participates in fat metabolism in storage of fat and oxidation of fatty acids, but no tests are available to assess the functional activity of the organ in this regard. Attempts made experimentally with fat tolerance tests have not proved successful.

The presence of bile in the gut is essential in emulsification and solvent action for the efficient digestion and absorbtion of fat. When bile is excluded by complete obstruction of the biliary tract, fat appears in the stool as neutral fat, soaps and fatty acids and contributes to the clay colour.

Protein Metabolism

The liver is essential for the deamination of amino acids and the formation of urea. In parenchymal disease, decreased urea formation and increased amino acid level in the blood would be expected, but these have not been uniformly observed. Several tests have been offered, as the examination of the amino nitrogen content of the urine after ingestion of 50 grams of gelatin, but the validity and usefulness of these tests have yet to be established.

Bile Acid Formation

The bile acids are formed in the liver and attempts have been made to measure the functional state of the organ by quantitative determination of them in the bile withdrawn through a duodenal tube. The technical procedures are not easy and the function has been found significantly diminished only in the end stages of liver disease.

Detoxification

The liver serves an important function in rendering inocuous a variety of toxic substances; it plays a primary role in the removal and destruction of alkaloids; it is concerned in the detoxification of cincophen by oxidation; various inorganic poisons are conjugated with bile acids to form inert or relatively insoluble salts.

The detoxifying function which has been measured is the conjugation of benzoic acid with aminoacetic acid to form hippuric acid which is excreted in the urine. The *hippuric acid test* is performed by giving 6 grams of sodium benzoate one hour after a light breakfast; the bladder is emptied and the urine specimen discarded; the urine is collected for the next four hours and the quantity of hippuric acid excreted determined. Patients with disease of the liver parenchyma excrete less than 3 grams in the four hour period.

Haemorrhagic Diathesis

The tendency of some jaundiced patients to bleed post-operatively has been a major surgical problem. It has been attributed variously to deficiency of calcium, fibrinogen and platelets and to the presence of cysteine. It is now considered due to lack of the fat soluble vitamin K, which is widely distributed in foods, but which being fat soluble, is not absorbed when bile is excluded from the gut; deficiency of vitamin K leads to deficiency of prothrombin and this is manifested in the tendency to bleed and in increased *prothrombin time*. It is relieved by the ingestion of bile or of bile and vitamin K.

Miscellaneous

Other abnormalities may be found in liver disease but the physiological and pathological processes involved are still obscure; some are considered to be of value in differentiating liver diseases, others are but of passing interest clinically.

It has been found that the level of *blood cholesterol* and the proportion of the free to the esterified form are altered in liver disease and also in other conditions. In obstructive jaundice there is a hypercholesterolemia paralleling the hyperbilirubinemia; in the jaundice of acute degeneration the blood cholesterol is lowered, particularly the ester fraction which may be reduced to traces. There is not alteration in Laennec's cirrhosis, cholecystitis or cholelithiasis if no obstruction is superimposed.

The *serum phosphatase*, determined by the amount of inorganic phosphorus liberated by the action of the blood enzyme on a phosphoric acid ester substrate, has been found experimentally and clinically to be greatly elevated in obstructive jaundice, mildly in hepatic jaundice and normal in haemolytic jaundice. The level is normally higher in children; it is raised most marked-

ly in hyperparathyroidism, rickets and osteomalacia.

The *plasma proteins* are found to be altered in patients with chronic parenchymatous liver disease. The total level is reduced and the albumin-globulin ratio is reversed.

The *Takata-Ara reaction* is the precipitation which occurs when sodium carbonate, mercuric chloride and acid fuchsin are added to the serum. It is found to be positive in cases of moderately advanced cirrhosis, and is stated to be useful in the recognition of this process.

Macrocytosis, an increase in the diameter but not the thickness of the red cell, has been reported in cases of long standing liver disease.

Discussion

It may be said generally of these tests of liver function that while they distinguish between disease processes in averages they cannot be relied on in individual cases; there is overlapping of the extreme findings between the groups of normal subjects and of patients with specific liver diseases.

The tests have been found more useful in following the course of diseases by repeated observations, than in aiding diagnosis.

Considering the diversity of function of the liver and the great physiological functional reserve, a battery of tests would be expected to be more reliable than individual tests; the tests of bilirubin metabolism and the galactose tolerance seem the most valuable ones to include.

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Feature Section

J. C. McCULLOCH, EDITOR

A CHOLERA EPIDEMIC IN CHINA

By J. R. LIND, M.D.
Kongmoon, South China

One of the few diseases really feared by the peoples of the East is Asiatic Cholera. It sweeps in pandemic waves, in cycles of every three years in India and every five years in China. The home of Cholera is the Lower Bengal and there it has probably been endemic from remotest antiquity. However, in the nineteenth century it began to extend all over Europe — even to the borders of the British Isles — and by land and water to China and Japan. The epidemic of 1870-3 was known to spread to the United States of America. It also follows in the wake of war. The present war in the east has already seen two severe outbreaks.

The disease is seasonal and seems to require a humid and warm climate. In China it generally occurs in the late summer and rapidly clears when the weather becomes cool and the atmosphere dry.

A very severe epidemic swept across China, from the shipping routes on the coast as far as Manchuria. This was the late summer of ninteen thirty-two, therefore we expected it to follow the usual cycle and appear in the summer of nineteen thirty-seven. Unfortunately we were not to be disappointed. When that summer was well advanced we received news of cases of Cholera at Macao, the Portuguese port on the coast forty miles from us at Kongmoon. Soon some cases were reported in nearby Canton City. Since there was a steady flow of river traffic between these cities and Kongmoon. we felt that our turn was next.

I will always remember our first case. We were watching the long stream of picturesque Chinese junks, that had been travelling all night on the West River from Canton. Silently, in mid-stream, while on the run, passengers were unloaded. The junks did not stop at our colony which was five miles above Kongmoon Port, their final destination. As the passengers scrambled ashore from the smaller boats we could see a group of people helping a man who seemed to be working under difficulties. However, he managed to walk and with a slow and deliberate footstep led this group towards our gate. The expression on his face I will never forget — it was ghastly — of a dusky, vivid hue. Truly a death mask if there ever was one. We found he was perspiring, yet his skin was cold and clammy. Although acutely conscious of what was going on, nevertheless he died a few minutes after he entered the hospital. On questioning his friends we gathered a text book picture of the typical history of Cholera. In the early hours of that morning he had taken sick with what was thought to be food poisoning or an ordinary diarrhea, which are very common during the summer months, in the tropics. However, before long he was passing the rice water stools that typify Cholera. After four or five hours the patient was complaining of pains in his limbs that were rapidly becoming worse and spreading up over his abdomen. When he arrived at the hospital he was suffering from severe abdominal pains which indicated impending death. On examination we found that his feet and hands showed, what we were soon to learn was most typical

of the disease (even more so than the rice water stools), that the skin was a dead white and in folds as if it had been soaked too long in water. The "wash-woman hand" is what some call it.

In the next few days we admitted six more cases. All but one died. In a country where there are many superstitious people who fear even the word death, it was not long before our hospital was rapidly emptying of the other patients. It looked as if we would have had nothing but a morgue on our hands. The question was whether to turn away all Cholera patients, or admit them and take a chance on our hospital becoming nothing much better than a morgue; not exactly a pleasant prospect. The situation was desperate for none of us had had to deal with such an epidemic before. Fortunately we were able to find, in our very limited library, the report of a symposium on Cholera held by foreign trained Chinese doctors, from Manchuria and North China, in Shanghai, after the epidemic in nineteen thirty-two. They had improved upon Sir Leonard Roger's technique. He had used hypertonic saline with considerable success, several years previously, while working in India. Due to the severe vomiting and diarrhea there are frequently present either an acidosis or an alkalosis with ketosis. Two solutions were suggested in their report. These were:

I. Sodium Bicarbonate....Grains 160
Sodium Chloride ..... Grains 60
Water to .....1 pint

II. Sodium Chloride ..... Grains 120
Calcium Chloride ..... Grains 4
Potassium Chloride .... Grains 6
Water to ..... 1 pint

For simplicity we termed them Cholera Solution Number I. and Cholera Solution Number II. From the time we started to use these solutions intravenously our mortality rate showed a spectacular drop. The treatment is probably one of the most fascinating that medicine has to offer to the world. At the first of the epidemic the patients were practically all moribund when brought to us. They would be literally dragged in and flopped down on the floor just inside the front door. Those that came with the patient were often so terrified by the speed with which their relation or friend had been stricken that they were ready to run as soon as they had left the patient. This is opposite to their usual custom of standing by their own people. Often we had to compel them to remain and see what the outcome would be. Frequently the patient would be pulseless at the wrist. If they were still breathing then we would admit them. The hospital staff were organized to work in teams—one doctor and two nurses, equipped with several intravenous outfits, would commence intravenous treatment almost immediately the patient was inside the front door. Time was the important factor. Speed and more speed was urged upon us all, if lives were to be saved. The usual routine was an intravenous running into each arm, and an interstitial of a 1,000 c.c. at the same time. It was nothing short of phenomenal the rate at which these patients could take fluid in large quantities. We would frequently give solutions at the rate of a pound every five minutes and often up to a total of two litres. When one saw the condition of the blood one realized the urgency for fluids. It was generally very small in total amount and of a dark viscid state with a high specific gravity. Evidently there is a massive flow of body fluids into the intestinal tract. This may take place so rapidly and the toxins be so great as to paralyze the intestine so that the patient dies without having a bowel movement. This is called Cholera Sicca.

In the larger hospitals where they had equipment they were able to give more careful treatment by constantly following blood chemistry and specific gravity. Due to our lack of equipment and limited staff we were able to watch

only the pulse and the blood pressure. The latter drops rapidly and a systolic below seventy we found was a grave sign.

Being unable to observe the blood chemistry it was a matter of guess work as to how much of the two solutions, mentioned above, we were to use. Nevertheless we worked out a rough ruling of using one pound of No. 1 solution to two pounds of No. 2 solution. This seemed effective in a large percentage of cases. By mouth we gave Fuller's Earth in massive doses until they were passing it in pure form by bowel. The books recommend many solutions which can be given by mouth. Unfortunately most of them aggravate the vomiting. Injections of morphine helped considerably. Keeping the body warm was also an important part of the treatment.

In spite of our many shortcomings, the treatment worked wonders. To watch a patient (one that you felt certain must be hopelessly gone) come back to life, gave us all a great thrill. What frequently happened was that from five to ten minutes after starting intravenous treatment on a patient, in which it was impossible to palpate a pulse at the wrist, the pulse could be quite easily felt. Then shortly afterwards the colour would start to creep across the cadaverous face. The patient would begin to show life once again. Often they would be conscious within half an hour from the beginning of treatment and not infrequently well enough after an hour to sit up and talk. Their first words were generally of sincere gratitude. A great many would tend to relapse a few hours later and the same treatment would have to be repeated. On one patient we had to repeat the treatment four times in twenty-four hours. We gave him twenty-four pounds of our Cholera solutions before he was able to build up some resistance to his infection. The occasional patient seemed to find it impossible to build any resistance. As there have been no antitoxins found to combat the toxins, our treatment was of little use in these cases.

The most feared complication was anuria. Of course giving hypertonic saline solutions, and in such large quantities, was tempting trouble with the kidneys. We would change to equal quantities of normal saline and glucose together, as soon as we thought it possible. Then to a 5% glucose solution. As a stimulant and diuretic we gave Caffeine Citrate gr. v. The prognosis was worse when the patient was pregnant or in either extreme age group.

The fame of the new cure spread far and wide and we were literally swamped with patients. Even the admitting rooms were turned into wards. After several weeks of sixteen to eighteen hours' work a day we found that our total number of patients came to several hundred. Our mortality in uncomplicated cases was 15% and in complicated cases 17%. This compared very favourably to an approximate 85% mortality in untreated cases.

The epidemic swept through China and the people died like flies—many collapsing on the streets. Coffins soared in price and were often unobtainable. It was easy to see why such a disease strikes fear into the hearts of the people. This all happens because they are ignorant of the fact that there is a vaccine that gives good protection. Unfortunately this vaccine is still too expensive for the average person. Nevertheless we were able to inoculate many hundreds. As the Comma Bacillus or Cholera vibrio can only enter by the mouth, it is felt that teaching a few hygienic principles (plus the very effective inoculations) will in the not too distant future, see this disease disappear from the face of the earth.

C.A.M.S.I. NOTES

By D. H. COPP, '39

Annual Convention of the Canadian Association of Medical Students and Internes, Toronto, Feb. 4-5, 1939.

(1) **Convention**: The second convention of the National Committee of the CAMSI was held at Toronto on the week end of Feb. 4, under the auspices of the University of Toronto Medical Society, and the local CAMSI Committee. Student and Interne delegates were present from seven of the nine Canadian Medical Schools, including Laval, Manitoba, McGill, Montreal, Queen's, Toronto, and Western. In addition, a number of Toronto medical students attended as observers. Official sessions were held in Hart House Saturday afternoon and all day Sunday, with Mr. Paul McGoey, President of the National Executive, presiding. The convention was opened with an address by the president, outlining the origin and progress of the CAMSI since its inception last spring. After the conclusion of the official session on Sunday, the delegates were all invited to supper by Sir Frederick Banting.

(2) **Reports**: Delegates from each school presented reports from their local committee on Student Health, Tuberculosis, prices of books and instruments, and Interne conditions in their respective centres. They outlined the local activities of the CAMSI, and spoke of the enthusiastic support of the faculty and students.

(3) **Tuberculosis**: Mr. McGoey presented a general report on tuberculosis, and spoke of the progress already made in introducing routine methods for early diagnosis. Methods of decreasing the risk of exposure of medical students and internes were discussed. The following resolution was passed: "Be it resolved that steps be taken to cut down the risk of exposure to tuberculosis of medical students and internes, and that this take the following form:

(a) Wearing of masks by all patients with tuberculosis, or suspected of tuberculosis, during examination.

(b) Isolation of tuberculous patients, until proven to have negative sputum.

(c) Instruction of students in proper precautions when examining a patient with tuberculosis, or suspected tuberculosis.

(4) **Constitution**: Mr. Copp presented a Constitution which, after minor modifications, was adopted subject to ratification by the individual medical societies. The essential points in the Constitution are as follows:

Name: The Canadian Association of Medical Students and Internes.

Aims: To further the welfare and interests of Canadian Medical Students and Internes, to promote co-operation between them and the medical faculties and hospital staffs, and to provide a medium for interchange of ideas between the Canadian medical schools.

Languages: French and English shall be the official languages.

Membership: Shall be open to all students in Canadian Medical Schools and internes in Canadian Hospitals.

All members in good standing of undergraduate medical societies belonging to the CAMSI are automatically members of the CAMSI.

The same applies to internes in hospitals in which there is a CAMSI Committee.

Local CAMSI Committee: The organization of the local CAMSI Committee shall be at the discretion of the local undergraduate medical society. The executive of this local committee shall consist of a Chairman and Secretary chosen from the clinical years of the medical course, and an Interne-Chairman to represent the internes in that region. At least one of the mem-

bers of the local executive must also be a member of the executive of the local undergraduate medical society.

National CAMSI Committee: This shall be the governing body of the CAMSI, and shall consist of two students and one interne delegate from each medical school in the CAMSI, along with the National Executive. It shall meet in convention at least once a year. It shall elect the National Executive, composed of a President, Vice-President, and Secretary-Treasurer. These latter must all be resident in one city during their term of office, which runs from July 1 to June 30.

Finances: An annual assessment, not to exceed 5c. per capita, may be levied by the National Committee, the assessment to be collected by the local undergraduate medical society or local CAMSI Committee.

Advisory Board: Outstanding members of the faculty or of the medical profession shall be chosen to form an Advisory Board. The Chairman of the Advisory Board shall be the Honourary President of the CAMSI.

(5) **Advisory Board**: Each delegation presented two names for the Advisory Board. Those from Toronto were: Dr. S. E. Ryerson, Assistant Dean. Dr. H. Agnew, Dept. of Hospital Service, Can. Med. Assoc.

Sir Frederick Banting was appointed Chairman of the Advisory Board.

(6) **Co-operation with the A.M.S.**: A resolution was passed sending greetings to the Association of Medical Students, as a body with like problems and aims, and advocating as close co-operation as possible in all kindred fields. More specifically, it was suggested that this co-operation take the form of:

Co-operation between committees studying similar problems.

Distribution of the "Journal of the A.M.S.," and contribution of a bilingual CAMSI page.

Exchange of delegates to conventions.

(7) **Canadian Interne Board**: One of the most constructive proposals considered at the convention was the scheme for interne appointments presented by Mr. Kerr, and developed by him in conjunction with Dr. Agnew of the Department of Hospital Service of the Canadian Medical Association. The purpose of the scheme is to remedy the present confused and unsatisfactory state of interne appointments by having all appointments made on a uniform date, and clearing all the appointments through a central Canadian Interne Board.

This board shall consist of a Chairman, representing the medical profession, who shall be the secretary of the Department of Hospital Service of the Canadian Medical Association, a Secretary, representing the hospitals, and an Associate Secretary representing medical students and internes, who shall be appointed by the National Committee of the CAMSI.

Prospective internes shall apply to various hospitals as at present, but shall also send a list of the hospitals to which they have applied, listed in order of preference, to the Canadian Interne Board. Applications shall be in by Oct. 15.

Hospitals will list the applicants in three categories:

First, a list of appointments, not to exceed the number of internships available.

Second, a reserve list, in order of preference, in case, with adjustment, there be vacancies left in the first list.

Third, a list of applicants specifically not desired.

Appointments shall then be mediated as follows:

All applicants on the first "appointed" list shall be appointed to that hospital, except that if an applicant is on the "appointed" list of more than one hospital, his choice from these hospitals as indicated by his order of preference, shall prevail.

Any gaps left in the first "appointed" list by this, shall be filled by those ranking highest on the second "reserve" list, and the appointments shall be mediated as above. This

may be repeated until all appointments are made.

Final appointments shall all be made on a uniform date.

It is felt that this scheme should help to remedy many of the existing drawbacks both to hospitals and to prospective internes. Its institution and success depends entirely on the support of the hospitals, prospective internes, and the Canadian Medical Association.

The plan as outlined was unanimously adopted by the convention, and a Committee on Interne Appointments, with Mr. Kerr as chairman, was appointed to co-operate with Dr. Agnew in furthering the scheme.

8. **Committees.** The following committees were appointed:

(a) Book Co-operatives—McGill and Montreal.
(b) Publications—Laval and Western.
(c) Interne Welfare—McGill and Montreal.
(d) Interne Appointments, Toronto.
(e) Tuberculosis—Toronto.
(f) Student Health—Manitoba.

(9) **National Executive:** The National Executive for the term July 1, 1939, to June 30, 1940, was chosen from Queen's.

President: Cyril K. Brown.
Vice-President: Hugh McGill.
Secy.-Treas.: H. Garfield Kelly, 397 Brock Street, Kingston.

(10) **Quebec Convention:** In connection with the Tercentenary Celebration of Hospitalization in Canada, at Quebec, a special CAMSI Convention is to be held there in August under the auspices of the Laval CAMSI.

Post-Convention Activities at Toronto.

At the recent medical elections, an innovation was introduced by having the vice-presidents of each year also elected as the year CAMSI representatives. A meeting of this CAMSI Committee-elect was held on Feb. 24, at Hart House. The following committees were appointed:

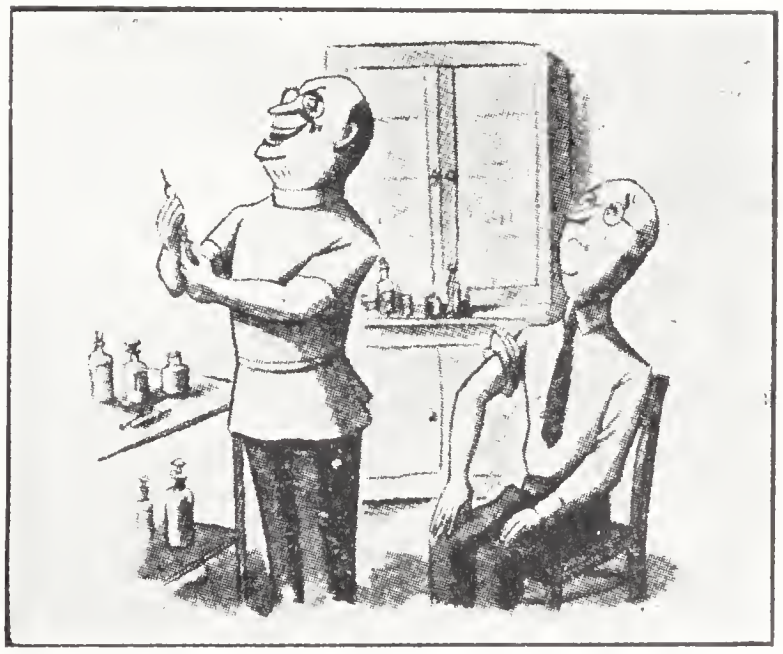
(a) Student Health — Hisey and Armstrong.
(b) Publications—Denne and Anglin.
(c) Book Co-operatives—Ortved and Routley.
(d) Tuberculosis—Caven.
(e) Canadian Interne Board: McGoey, Kerr, Ortved.

The executive of the local CAMSI Committee wes elected by the year representatives as:

Chairman: Hisey.
Secretary: Denne.

All who are interested in the CAMSI, or in any specific committee should get in touch with the committee.

MEDICAL MANNERS



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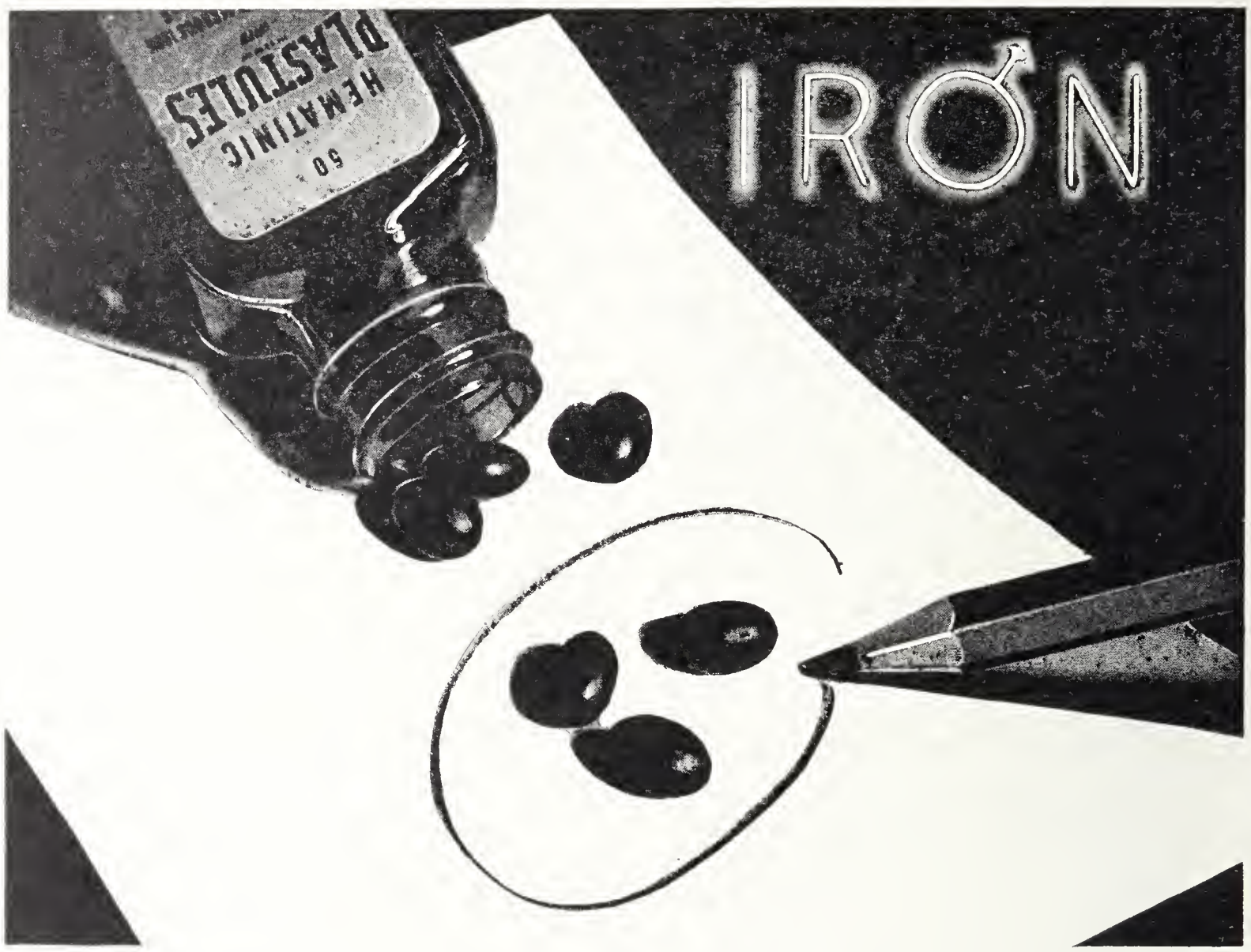

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Medical Society Notes

BILL ORTVED, Secy.-Treas.

As usual the first two months of the new year have been packed full of activity for the Medical Society. Most of January was taken up with preparations for the Medical At-Home, which showed the extensive work expended on it by being an outstanding party. Bunny Berigan, the band from the States, though a little tardy in arriving for the party, made up for lost time once started, and carried on into the wee small hours. There are some who thought Berigan played at too fast a tempo—there are likewise some who thought he didn't swing it enough; but the great majority, according to calculation, thought he played just about right. It is well nigh impossible to please everyone exactly, as far as the music is concerned, but certainly in this case the party left little to be desired.

The Canadian Association of Medical Students and Interns held its annual convention on the fourth and fifth of February, in Hart House. To this conference seven of the ten medical schools in Canada sent delegates. A great deal was done in this limited time. The most important events were the adopting of a constitution, the plan for intern appointments which is to be given to the hospitals this summer for their approval. The comparison of the book prices in different schools was made, and a committee set up for the investigation of these prices. Tuberculosis and general student welfare were discussed, and plans made for a more extensive investigation of these subjects in the different universities and nearby hospitals during the coming year. A number of other important problems were taken up in addition. A complete report of this conference along with the accepted constitution, will be forthcoming soon. It is expected that there will be an organization meeting within a few weeks, to get the C.A.M.S. & I. on this campus into a more concrete form. The basis for this organization will be the vice-presidents elect, of the respective years. The following three men have kindly consented to act as an advisory board for the C.A.M.S. & I. on this campus, and each of them so far has given invaluable assistance.

Dr. E. Stanley Ryerson—Assistant Dean of the Faculty.

Dr. Harvey Agnew—Secretary of the Canadian Medical Association.

Sir Frederick Banting.

Daffydil was the next event on the medical calendar. This year in keeping with tradition, it ran for three full nights and gave evidence of great planning and real originality, with the final result—a show of no mean calibre. As Charlie Sheard, the chairman of the committee, had the misfortune to be the possessor of an acute appendix early in February, he had to leave the production of Daffydil in the hands of Berni Laski and John Rathbun, who took over very efficiently.

Then finally the Medical Society elections on February the seventeenth. These were run off with the usual platforms, promises and propaganda and close competitions for the various offices. The Medical Society for the next year is headed by Bill McGill, and the Medical Athletic Association by Aub. Boyd. Under these two men things should run smoothly and efficiently during 1939-40, as far as the male aggregation of the faculty is concerned. Helen Holden was chosen to guide the fate of the Medical Women's Undergraduate Association in the ensuing year.

Medical Athletics

M. P. TOWNSEND.
Secretary-Treasurer.

Since the last article things have taken a turn for the worse and even now the prognosis is far from good. With our surprise victory in soccer as the last bright spot in an otherwise dreary post-Mulock doldrums, our teams have met consistently with close but none the less conclusive setbacks.

The Soccer Team, although not the most skilful in the league, made up for this handicap by a surprising show of spirit. Surprising because it has been a thing unknown for several years. Also the judicious application of superior weight helped considerably.

Our three volleyball teams finally succumbed without one winning a group title. The high hopes for the Seniors were dashed by the hard fighting U.C. team. While the other teams never did get far out of the ruck.

Basketball again appears to be the most popular sport with one more team entered this year, raising the grand total to four. It would be nice to have four Med. Teams in the playoffs this year and keep up the good showing made last year. Unfortunately the Srs. have only a mathematical chance in their groups, having lost one and tied one.

The Hockey teams are well along in their schedules and at present the Seniors appear to be in a promising position to win "C" Groups, having lost only one game to date and are leading the group.

The Juniors however ran into rather fast company and haven't been able to register a victory as yet.

Baseball is well on its way and at present the Seniors haven't lost a game in five starts and are as a result leading their group by a promising margin. It would appear that they will have a chance of avenging the playoff losses of the last two seasons.

The Juniors are second in their group and have high hopes of yet reaching the playoffs.

If the ladies will again forgive us for placing them at the foot of the list we would like to give them a boost for their Hockey victory against St. Mike's girls. It might be interesting to have a three team playoff for faculty Hockey Champions. If the ladies are interested we would gladly act as intermediary.

The present standings in the Reed Trophy are out and after winning two Interfaculty Championships we have only improved our lot by two positions. The lowly position of last in the first division (namely seventh) is rather a bitter mouthful to have forced on us. Once more the idea arises that either the Intramural point system is at fault or we as a faculty are following the wrong tactics in competition.

As it now stands Meds are above average in team competition and far below average in individual competition. However, the point system as it now exists makes little differentiation between a team and an individual championship. Since we are admittedly weak in individual sports our only alternative, (having failed to drum up enthusiasm in this line) would be to enter more teams. This sounds very simple as we have a comparatively large faculty and therefore considerable material. However there is one negative factor — Money. Despite the dollar and a half collected from each student, our time honoured habit of having each player keep his uniform at the end of the season soon makes serious inroads on this apparently large sum. This year, loss in income due to decreased enrolment and the turning of the girls donation, rightfully, into their hands coupled with the added expense of additional teams has taxed our resources to the utmost. Therefore if we wish to carry out the above suggestion of more teams we have two alternatives to follow.

The first is an increased athletic fee. This would appear unsatisfactory

to most students under the present general rise in fees and tuition coupled with the fall off in general countrywide earning power.

The second suggestion is one already practised by most of the faculties on the Campus. Namely the calling in of uniforms at the end of the season. This suggestion may be also unsatisfactory to many as there is a feeling in some quarters of having earned a uniform by participating in the said sport. A possible consideration might be shown by allowing graduating men and winning teams to keep their uniforms or by giving a graduating man some worth while token for having played a required number of years.

Be that as it may, the present intramural point system is so arranged as to give only the Faculty with a goodly proportion of their members playing a possible chance to win. Therefore we must follow one of the above plans or give up hope of making a creditable showing in the Reed Trophy Competition. May we suggest that the above suggestions be seriously considered by the students and if sufficient interest is shown a general vote would be the plausible step.

M. P. Townsend.

Book Review

HISTOIRE DE LA MEDECINE.

By Dr. Eugene St. Jacques. 221 *pages. Montreal. Edition Beauchemin,* 1935.

As Professor St. Jacques states, this book gives a bird's eye view of the history of medicine. The material is essentially that which he teaches his students at the University of Montreal.

Writing with typical French clarity and precision he divides medical history into ten definite periods which he puts forth in twenty-six chapters. These chapters are crammed with discoveries and dates giving an excellent general idea of the evolution of medicine from the earliest and simplest stages to the extremely complex system of specialized medicine we have to-day.

In Babylonia the priesthood also practised medicine; they claimed diseases were caused by demons. Egyptians sometime later understood the importance of the heart and lungs in maintaining life. Medicine was not without dangers in those days. Assyrian physicians who lost patients risked having their hands cut off.

Hippocrates then laid the foundation of modern medicine. He described a large number of diseases and taught the importance of proper examination. The Romans, of practical mind, concentrated on surgery and public health.

Then the mediaval schools of Italy were founded. Ambrose Paré ligated vessels of amputation stumps instead of pouring boiling oil on them. Vesalius, the great anatomist, published "*de fabricus Humanus Corporis*" in 1543. Then leprosy, bubonic plague and syphilis over-ran Europe. Neapoliatans called syphilis "the French disease" and France claimed it came from Naples. Human nature still remains the same! The discovery of the circulation by Harvey, of the microscope and the intense study of physiology all lead to further work and greater knowledge. Virchow, Pasteur and Lister are all taken into account.

The kaleidoscopic advance of medicine gradually becomes more colorful and more complex. Dr. St. Jacques focuses the spotlight on discovery after discovery and finally compares the tremendously complex, highly specialized schools of the leading scientific nations of to-day.

In retrospect this volume reminds me somewhat of Ravel's "*Bolero,*" which starts with a single instrument on the simplest theme, and then gradually by addition of many more its rhythm becomes ever faster and more furious.

In short, an easy reading, concise and very enchanting volume. If you are interested in medical history and want to improve your French, by all means read it.

A.J.A.

A CLINICAL GUIDE TO MEDICINE.

By Alfred Auerback, M.D. 147 *pages.*

Alf. Auerback in his second edition of the "Clinical Guide," has followed the organization of the original. However, the new Guide is longer, parts formerly left out now are incorporated, and the contents of the first volume have been pruned or amplified as experience seemed to indicate.

The book is divided into two parts. The first one hundred and twenty-five pages have to do with treatment of various diseases. classifications for diagnostic purposes and descriptions of therapeutic methods. The remaining pages outline laboratory proce-

dures commonly done by internes. An excellent index is appended.

This book has been developed to set out, in a concise way, the exact therapeutic procedures commonly used in the various diseases. The author has succeeded admirably, and it would be hard to find another book where these necessary facts can be found more accurately and more quickly. While this book is not the panacea for all students' therapeutic headaches, yet as a constant, ready and stimulating reminder it seems unsurpassed.

Diagnostic classifications, descriptions of various therapeutic procedures and substances have been scattered through the first part of the book. Such material as vitamins, tonics, toxoid and vaccine therapy, etc., could probably well be collected together, leaving the first part of the volume unimpeded for descriptions concerned with particular diseases. More reference to the treatment of disease in children would increase the score and value of this work.

However, any criticism could only be on minor points. Those who wish for a handy, short reference—not a text-book—on therapeutics, will find this very satisfactory.

Abstracts

D. H. COPP, *Editor*

Contributors. L. J. Lester. R. L. McMillan. R. L. Sullivan. J. C. McCulloch. J. C. Rathbun. J. C. Watt.

EARLY MANIFESTATIONS OF PRIMARY CARCINOMA OF THE LUNG.

By L. A. Hochberg and M. Lederer—*Arch. of Int. Med. Jan.*, 1939.

An early diagnosis of carcinoma of the lung is important if therapeutic measures are going to be taken. A patient of the cancer age and showing a change of cough habit is suspicious. It is important to realize, however, that there may be no symptoms referable to the chest. The author considers the carcinoma from the aspects of etiology, age and sex. There are no symptoms that are pathognomonic of this condition. Symptoms are varied, for example, pressure on the vagus nerve may give rise to abdominal symptoms, hence, in abdominal cases where no signs are elicited examine chest. The pulmonary signs depend on whether the tumour growth is situated in the hilar or parenchymal or peripheral part of the lung. The reports of thirteen cases, in which there were no chest symptoms were given.

Comment:—Carcinoma of the lung must be ruled out in every obscure ailment by a more painstaking history-taking and a more careful physical examination.

Conclusion:—(1) carcinoma of the lung is not uncommon; (2) 22% of 60 cases had no symptoms referable to the thorax; (3) 82% of the cases were between 45 and 65 years of age; (4) the disease was four times as frequent in males as in females; (5) the final diagnosis rests with the microscopic observation of cancer cells in representative tissue; (6) there are no signs pathognomonic with carcinoma of the lung. Change in coughing and expectoration or paroxysmal dyspnoea require careful examination before carcinoma is ruled out; (7) accessory means of diagnosis, in order of importance.

(a) bronchoscopic examination plus biopsy.
(b) pleural effusion, to be examined for tumour cells.
(c) lung puncture.
(d) thoracotomy.
(e) biopsy of a metastatic nodule.

R.L.M.

A BIOCHEMICAL STUDY OF PATIENTS ON SULPHANILAMIDE THERAPY.

By C. C. Lucas and D. R. Mitchell—*C.M.A.J., Vol.* 40, *No.* 1.

This paper is written primarily in an attempt to place sulphanilamide therapy on a rational and scientific basis. Single and multiple doses were tried in patients with normal and impaired renal function.

The larger the initial dose the more rapidly the peak is reached and the higher is the peak. It is extremely hard to raise the blood concentration above 4 to 6 mg.% in persons having normal kidney function until body saturation is attained, a process which takes from two to four days. Absorption may be favoured by administering the drug in solution or with large amounts of water.

In persons with impaired renal function the blood levels may rise to extremely high concentrations due to the impaired excre-

tion. The rate of excretion cannot be forecast reliably by any of the present renal tests and is found to vary greatly even in persons with apparently normal kidney function.

The rate of excretion does not increase with an increased fluid intake in subjects with normal renal function and therefore by restricting the fluid intake high urinary concentrations are attained which are suitable for urinary tract infections. Due to this finding doses of 5 to 20 grains given t.i.d. are all that is required.

The step-dosage procedure has been found very effective here. Small doses are given at first and gradually increased. This procedure avoids distressing toxic reactions but in this series was used only in urinary cases and therefore its value cannot be assessed in other diseases.

J.C.R.

NUTRITION IN TORONTO.

By E. W. McHenry—*C.P.H.J., Vol.* 30, *No.* 1.

This paper summarizes the findings in a study of a group of Toronto families with an average income of $19.64 per week. Diet was found to be substandard in men, women, and children, in calories, protein, iron and calcium. Diet in the males more nearly approached the Canadian Dietary Standards. Children were found especially, to be getting diets low in calcium and iron, the average intake of milk being 4/10 of a pint a day. In general the diet was more satisfactory where the income was larger but examples were found of families which received excellent nutrition on smaller incomes. This is due to the ability of some women to choose food wisely and economically. As a result more time should be spent on educating mothers along these lines. As "the welfare of a nation depends on the way in which it is nourished," every student should read this enlightening article.

J.C.R.

EMPYEMA.

By W. G. Carscadden—*C.M.A.J., Feb.*, 1939, *Vol.* 40, *No.* 2.

This paper is a review of 83 cases of acute empyema, not including tuberculosis, treated at St. Michael's Hospital over a ten-year period.

Etiology—Pneumonia accounts for 84% of cases and adjacent abscesses for most of the remainder. The responsible organism was pneumococcus in 36, streptococcus in 28, and staphylococcus in 6. The organism was not necessarily the same as that found in the sputum.

Pathology—The picture varies with the causative organism. Those following pneumonia may be divided into two types—metapneumonic empyemas appearing after the pneumonia has subsided, due to pneumococcus with thick pus, and synpneumonic empyemas occurring early in the disease, due to streptococcus with thin pus.

Mortality—This was 16.7% but 78.5% of deaths were mainly due to the original disease and not to the empyema.

Treatment—Closed drainage was used for synpneumonic cases, cases with large exudates and those due to sudden rupture of a lung abscess with a large pyopneumothorax. Closed drainage was preferably by repeated aspirations or intercostal stab, the former being the initial step in all streptococcal infections. After-care consisted of irrigation with Dakin's solution except where bronchial fistula existed. Small blood transfusions aid in increasing the general well-being.

J.C.R.

SELF-INDUCTION ANALGESIA WITH NITROUS OXIDE FOR UROLOGIC EXAMINATIONS AND MINOR PROCEDURES.

By Hugh H. Young—*Journ. of Urology, Vol.* 41, *No.* 1.

This article points out how local urethral anaesthesia is frequently unsatisfactory and painful. It is often necessary to administer spinal anaesthesia. It is therefore desirable to obtain a light and safe method of analgesia.

In 1936 Dr. J. A. Heidbrink, a dentist, developed a simple apparatus for self-administration of nitrous oxide. This machine allows the patient to pump a nitrous oxide and air mixture into the usual bag. On cessation of pumping the mixture in the bag will become progressively weaker so that should the patient anaesthetize himself to the point of unconsciousness the flow of nitrous oxide stops and the patient will come out of the anaesthetic. Then on the return of pain he may again induce analgesia. This apparatus is on sale on the open market but no report of the machine has appeared in the journals.

This apparatus has proved extremely successful for urological procedures.

J.C.R.

PHYSICAL AND TOXIC FACTORS IN SHOCK.

By Frederick M. Allen, M.D., *New York. Archives of Surgery, Vol.* 38, *No.* 1, *January*, 1939.

Shock is of two types:

(a) Primary shock arising reflexly from neural injury resulting in a clinical syndrome associated with low blood pressure.

(b) Secondary shock which is slower

developing, and characterized by reduced plasma volume and increased concentration of the blood due to the migration of fluid into the tissues.

The author obtained primary shock experimentally in rats by dissecting out both Sciatic nerves and pinching them distally. The rats showed evidence of shock but the blood counts never changed.

Secondary shock was obtained by an elastic tourniquet around the upper thigh in rats for three to five hours. If the tourniquet was on for three hours all the rats recovered but if on five hours all rats died from shock if not treated. Death resulted from apnoea, the heart continuing to beat after respirations had ceased from a few seconds to a few minutes.

Death from secondary shock could be prevented by amputation of the asphyxiated pad within one to three hours of releasing the ligature or by transfusions of whole blood, plasma or saline. In this connection it is interesting to note that transfusion from donor rats already dying of shock was practically as effective in saving life as the blood from normal animals. This discounts the theory of a toxin in the circulating blood being responsible for secondary shock. However after more extensive tissue damage (e.g. asphyxia of more than one limb for five hours or of one limb for seven or eight hours) transfusions no longer saved life although they restored normal blood volume. Simple saline did cause some to recover under the same conditions and hence the author believes that there is a "tissue thirst" "an obligatory edema" or an avidity of tissues and that a fluid that can easily pass through the cappillary is indicated.

In conclusion Dr. Allen states that secondary shock being radically different from primary shock could better be called "histotoxicosis" and three degrees recognized.

(1) Small local injury resulting in tissue injury with liberation of a histamine like substance and vaso-dilation in the area, but no constitutional effects.

(2) More severe injury with elaboration of more "histotoxin" which causes not only increased local transudation from the capillaries but also throughout the body and can be cured by the administration of sufficient fluid.

(3) Still more extensive injury which is fatal in spite of preserving the fluid balance. This is sometimes seen after diabetic coma when fluids have been pushed and the blood sugar returned to normal for some hours yet the patient dies in shock.

R.L.S.

THE USE OF FREE FULL THICKNESS SKIN GRAFTS.

By J. Eastman Sheehan, M.D.,*New York—Jour. A.M.A., Jan.* 7, 1939.

A primary consideration when skin is to be replaced, especially on the face, is that the new skin will conform to its surroundings in texture, in surface level, and in coloration and will incorporate imperceptibly with the adjoining skin. A pedicle flap leaves a visible disfigurement. The thin epidermic graft is too thin to maintain the surface level of its surroundings and tends to become brownish colored. The tubed pedicle graft undergoes changes in its fat and fibrous tissues, after it is tubed, which change its texture. The free full thickness graft has none of these disadvantages.

For successful application of the free full thickness graft the following procedure should be adhered to:

(1) The skin should be in a healthy state. This applies not only to the immediate vicinity of the area from which the graft is to be taken but to the body generally. Some of the deterrent conditions are diseases that would effect the health of the skin. Pimples are a danger sign and suggest delay until improvement has been effected. Concealed infection can be detected by the Schilling test, since in the presence of infection there are more immature neutrophils in the blood. If the platelet count is very low there will be oozing from the bed on which the graft is to be placed, and this will interfere with the growth of capillaries into the graft.

(2) The graft area itself demands respect. Since cleansing the skin reduces the amount of oxygen and sulphur in the skin, and thus lowers the vitality of the cells, the skin is washed the night before operation.

(3) A dry base at the defect area is absolutely essential. The vessels in the base are tied with the finest Deknatel silk. All blood clots must be removed.

(4) In taking the graft the lines of skin tension should be respected. The graft should not have bevelled edges, and should be cut slightly smaller than the defect so that it is put on the stretch when sutured. It is not washed in saline or other solution, since its own serums aid in countering infection, and insure adhesions between the graft and the base.

(5) The lowest densest subcutaneous layer of the graft is removed to aid restoration. This seems to allow better permeation with lymph fluid and more rapid growth of capillaries into the graft. The graft is immobilized by a mold or stent supported by an outer frame of celluloid. The mold serves to put pressure on the graft. Too much pressure impedes the

growth of new capillaries, and too little pressure disturbs the adherence of the graft to the base.

If signs of shock toxemia appear all food should be stopped and intravenous glucose given. J.G.W.

CLINIC OF DRS. ITALO F. VOLINI AND WILLIAM W. SHAPIRO

Cook County Hospital and Department of Medicine, Loyola University School of Medicine. Medical Clinics of North America, Jan. 1938.

Primary Carcimona of the Lung

Primary bronchogenic carcinoma is very common. It has shown a real as well as an apparent increase in the last three decades. At Cook County Hospital it is the third most frequent type of primary cancer, being exceeded in incidence only by carcinoma of the stomach and intestines. The increased longevity of the present era, greater exposure to irritating vapors, increased use of tobacco may all be responsible for the greater incidence.

The onset of the condition is usually insidious, and the patient lives from one week to three years after the onset of symptoms, the average being one year.

Symptoms

The symptomatology of pulmonary neoplasm may be almost identical with that of tuberculosis, lung abscess, and other chronic conditions. Fever may be present. Hemoptysis may be the first symptom to attract attention. The haemorrhage may be massive, or it may occur in small amounts. Sputum is often blood-streaked, prune-juicy in character.

Chest pain is a frequent sign of lung tumour. It is stabbing or boring in character. The accumulation of large quantities of pleural fluid does not modify it, while in tuberculosis the pain is relieved.

Cough and dyspnoea are prominent, especially when bronchial occlusion with accompanying atelectasis is present. Cyanosis is observed in association with large atelectatic areas or with obstruction of the superior vena cava.

Cerebral symptoms often of a mental character may appear before lung findings can be discerned by physical, bronchoscopic or x-ray examination.

An individual forty-five years old or more who develops a subacute or chronic respiratory disorder in the absence of previous history may equally well have tuberculosis, bronchiectasis, abscess, or neoplasm. A patient over fifty will more likely have a neoplasm.

Physical Examination

Bronchus carcinoma is characterized by the paucity of findings in proportion to the extent of the pathological process. In central upper lobe involvement there may be no findings whatsoever. Examination of the chest reveals findings similar with those in tuberculosis, bronchiectasis, or abscess. In the presence of extensive infiltration in tuberculosis, the breath sounds are bronchial in type and vocal fremitus and vocal resonance are usually increased. The reverse is true in neoplasms due to the poor conductivity of carcinomatous lung tissue, a collapsed lobe with absent breath sounds is an important sign.

J.G.W.

VISUALIZATION OF THE CHAMBERS OF THE HEART.

By G. P. Robb and I. Steinberg.—*Am. J. Roentgenol., Jan.* 1939.

The authors describe a practical method of X-Ray visualization of the heart, pulmonary circulation, and great vessels, which has been successfully used in 238 instances. 25-40 c.c. of 70% diodrast is injected rapidly into an arm vein, and X-Rays are taken after a definite time interval. The latter depends on what part of the circulation is to be visualized, and upon the previously determined circulation time. Unpleasant reactions may occur after injections, but are not serious.

Contra-indications are nephritis, severe liver disorders, and hyperthyroidism. By using this method of visualization, it has been possible to determine the point of occlusion of the Superior Vena Cava, to study the vascular patterns of the lung, and most important of all, to reveal the internal structure of the living heart. Not only the size and shape of the chambers, but also the valves may be visualized. When fully developed, this technique promisess to be a great advance in aids to cardiovascular diagnosis. L.J.L.

ARTERIOLES OF PANCREAS, LIVER, GASTRO-INTESTINAL TRACT AND SPLEEN IN HYPERTENSION.

By C. G. Morlock. *Rochester, Minn.—Archives of Int. Med. Jan.*, 1939.

The arteriole, because of its pressure gradient, should suffer most in hypertension. However, many investigators have disagreed as to the relation of change in vessels to hypertension. The arteriole of pectoral muscle, taken from a hypertensive patient, was said by some workers to deviate from normal. Others said that the variation was within the range obtained from fixation of normal specimens. Mor-

lock studied a fairly large series of hypertensive vessels from the the pancreas, liver, gastro-intestinal tract and spleen obtained at autopsy. A similar series of controls was also studied. The sections were prepared by different stains and the results were analysed by a mathematical method. The basis of comparison was the ratio of wall to lumen.

Findings (1) There was no measurable change with age in the normal person.

(2) A marked thickening of the wall and a reduction of ratio wall to lumen was found in hypertensive patients of all ages. The degree of thickening was greater the more severe the hypertension.

(3) The arterioles in all organs examined were equally effected.

(4) Histological changes:

1. hyperplasia of muscle in media.
2. degeneration and fibrosis of media.
3. degenerative changes in the intima. In more severely damaged vessels, most of the wall is intima in this stage.

Conclusions. On the basis of this experiment and those of others, the author concludes that in hypertension there is a generalized alteration of the arteriolar system, uniform in character and degree in different organs but varying with the severity of the disease. The change is anatomical and can be measured. Whether this change is primary or secondary to the hypertension is unknown.

R.L.M.

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